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(54) Title: METHODS FOR OBTAINING PLANT VARIETIES

(57) Abstract

An isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide functionally involved in the DNA mismatch repair system of a plant.

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Methods for Obtaining Plant Varieties

TECHNICAL FIELD

The present invention relates to nucleotide sequences which encode polypeptides involved in the DNA mismatch repair systems of plants, and to the polypeptides encoded by those nucleotide sequences. The invention also relates to nucleotide sequences and polypeptide sequences for use in altering the DNA mismatch repair system in plants. The invention also relates to a process for altering the DNA mismatch repair system of a plant cell, to a process for increasing genetic variations in plants and to processes for obtaining plants having a desired characteristic.

BACKGROUND OF THE INVENTION

Plant breeding essentially relies on and makes use of genetic variation which occurs naturally within and between members of a family, a genus, a species or a subspecies. Another source of genetic variation is the introduction of genes from other organisms which may or may not be related to the host plant.

Allelic loci or non-allelic genes which constitute or contribute to desired quantitative (e.g. growth performance, yield, etc.) or qualitative (e.g. deposition, content and composition of seed storage products; pathogen resistance genes; etc.) traits that are absent, incomplete or inefficient in a species or subspecies of interest are typically introduced by the plant breeder from other species or subspecies, or *de novo*. This introduction is often done by crossing, provided that the species to be crossed are sexually compatible. Other means of introducing genomes, individual chromosomes or genes into plant cells or plants are well known in the art. They include cell fusion, chemically aided transfection (Schocher et al., 1986, Biotechnology 4: 1093) and ballistic (McCabe et al., 1988, Biotechnology 6: 923), microinjection (Neuhaus et al., 1987, TAG 75: 30), electroporation of protoplasts (Chupeau et al., 1989, Biotechnology 7: 53) or microbial transformation methods such as Agrobacterium mediated transformation (Horsch et al., 1985, Science 227: 1229; Hiei et al., 1996, Biotechnology 14: 745).

However, when a foreign genome, chromosome or gene is introduced into a plant, it will often segregate in subsequent generations from the genome of the recipient plant or plant cell during mitotic and meiotic cell divisions and, in consequence, become lost from the host plant or plant cell into which it had been introduced. Occasionally, however, the introduced genome, chromosome or gene physically combines entirely or in part with the genome, chromosome or gene of the host plant or plant cell in a process which is called recombination.

Recombination involves the exchange of covalent linkages between DNA molecules in regions of identical or similar sequence. It is referred to here as homologous recombination if donor and recipient DNA are identical or nearly identical (at least 99%

base sequence identity), and as homeologous recombination if donor and recipient DNA are not identical but are similar (less than 99% base sequence identity).

The ability of two genomes, chromosomes or genes to recombine is known to depend largely on the evolutionary relation between them and thus on the degree of sequence similarity between the two DNA molecules. Whereas homologous recombination is frequently observed during mitosis and meiosis, homeologous recombination is rarely or never seen.

From a breeder's perspective, the limits within which homologous recombination occurs, therefore, define a genetic barrier between species, varieties or lines, in contrast to homeologous recombination which can break this barrier. Homeologous recombination is thus of great importance for plant breeding. Accordingly there is a need for a process for enhancing the frequency of homeologous recombination in plants. In particular, there is a need for a process of increasing homeologous recombination to significantly shorten the length of breeding programs by reducing the number of crosses required to obtain an otherwise rare recombination event.

At least in *Escherichia coli*, homologous and homeologous recombination are known to share a common pathway that requires among others the proteins RecA, RecB, RecC, RecD and makes use of the SOS induced RuvA and RuvB, respectively. It has been suggested that mating induced recombination follows the Double-Strand Break Repair model (Szostak et al., 1983, Cell 33, 25-35), which is widely used to describe genetic recombination in eukaryotes. Following the alignment of homologous or homeologous DNA double helices the RecA protein mediates an exchange of a single DNA strand from the donor helix to the aligned recipient DNA helix. The incoming strand screens the recipient helix for sequence complementarity, seeking to form a heteroduplex by hydrogen bonding the complementary strand. The displaced homologous or homeologous strand of the recipient helix is guided into the donor helix where it base pairs with its counterpart strand to form a second heteroduplex. The resulting branch point then migrates along the aligned chromosomes thereby elongating and thus stabilising the initial heteroduplexes. Single stranded gaps (if present) are closed by DNA synthesis. The strand cross overs (Holliday junction) are eventually resolved enzymatically to yield the recombination products.

Although in wild type *E. coli* homologous and homeologous recombination are thus mechanistically similar if not identical, homologous recombination in conjugational crosses *E. coli* x *E. coli* occurs five orders of magnitude more frequently than homeologous recombination in conjugational crosses *E. coli* x *S. typhimurium* (Matic et al. 1995; Cell 80, 507-515). The imbalance in favour of homologous recombination was shown to be caused largely by the bacterial MisMatch Repair (MMR) system since its

inactivation increased the frequency of homeologous recombination in *E. coli* up to 1000 fold (Rayssiguier et al. 1989, Nature 342, 396-401).

In *E. coli*, the MMR system (reviewed by Modrich 1991, Annual Rev Genetics 25, 229-253) is composed of only three proteins known as MutS, MutL and MutH. MutS recognizes and binds to base pair mismatches. MutL then forms a stable complex with mismatch bound MutS. This protein complex now activates the MutH intrinsic single stranded endonuclease which nicks the strand containing the misplaced base and thereby prepares the template for DNA repair enzymes.

During recombination, MMR components inhibit homeologous recombination. In vitro experiments demonstrated that MutS in complex with MutL binds to mismatches at the recombination branch point and physically blocks RecA mediated strand exchange and heteroduplex formation (Worth et al., 1994; PNAS 91, 3238-3241). Interestingly, the SOS dependent RuvAB mediated branch migration is insensitive to MutS/MutL, explaining the observed slight increase in SOS dependent homeologous recombination. Homeologous mating even induces the SOS response, thereby taking advantage of RuvAB induction (Matic et al. 1995, Cell 80, 507-515).

The MMR system thus appears to be a genetic guardian over genome stability in *E. coli*. In this role it essentially determines the extent to which genetic isolation, that is, speciation, occurs. The diminished sensitivity of the SOS system to MMR, however, allows (within limits) for rapid genomic changes at times of stress, providing the means for fast adaptation to altered environmental conditions and thus contributing to intraspecies genetic variation and species evolution.

The important role of MMR in preserving genomic integrity has been established also in certain eukaryotes. In its efficiency, the human MMR, for example, may even counteract potential gene therapy tools such as triple-helix forming oligonucleotides including RNA-DNA hybrid molecules (Havre et al., 1993, J. Virology 67: 7234-7331; Wang et al., 1995, Mol. Cell. Biol. 15: 1759-1768; Kotani et al., 1996, Mol. Gen. Genetics 250: 626-634; Cole-Strauss et al., 1996, Science 273: 1387-1389). Such oligonucleotides are designed to introduce single base changes into selected DNA target sequences in order to inactivate for example cancer genes or to restore their normal function. The resulting base mismatches however are recognised by the mismatch repair system which then directs removal of the mismatched base, thereby reducing the efficiency of oligonucleotide induced site-specific mutagenesis.

To date, two families of related genes, homologous to the bacterial *Mut*S and *Mut*L genes have been identified or isolated in yeast and mammals (recent reviews by Arnheim and Shibata, 1997, Curr. Opinion Genet. Dev. 7, 364-370; Modrich and Lahue, 1996, Annual Rev. Biochem. 65, 101-133; Umar and Kunkel, 1996, Eur. J. Biochem. 238, 297-307). Biochemical and genetic analysis indicated that eukaryotic MutS homologs (MSH)

and MutL homologs (MLH, PMS), respectively, fulfil similar protein functions as their bacterial counterparts. Their relative abundance, however, could reflect different mismatch specificity and/or specialisation for different tissues or organelles or developmental processes such as mitotic versus meiotic recombination.

To date, six different genes homologous to *Mut*S have been isolated in yeast (y*MSH*), and their homologs have been found in mouse (m*MSH*) and human (h*MSH*), respectively. Encoded proteins yMSH2, yMSH3 and yMSH6 appear to be the main MutS homologs involved in MMR during mitosis and meiosis in yeast, where the complementary proteins MSH3 and MSH6 alternatively associate with MSH2 to recognise different mismatch substrates (Masischky et al., 1996, Genes Dev. 10, 407-420). Similar protein interactions have been demonstrated for the human homologs hMSH2, hMSH3 and hMSH6 (Acharya et al., 1996, PNAS 93, 13629-13634).

MutL homologs (MLH and PMS), recently reviewed by Modrich and Lahue (1996, Annual Rev. Biochem. 65, 101-133) have so far been found in yeast (yMLH1 and yPMS1), mouse (mPMS2) and human (hMLH1, hPMS1 and hPMS2). The h*PMS2* is a member of a family of at least 7 genes (Horii et al., 1994, Biochem. Biophys. Res. Commun. 204, 1257-1264) and its gene product is most closely related to yPMS1. Prolla et al. (1994, Science 265, 1091-1093) presented evidence for yPMS1 and yMLH1 to physically associate with each other and, together, to interact with the MutS homolog yMSH2 to form a ternary complex involved in mismatch substrate binding.

However, while medical interest in mismatch repair has prompted extensive research on MMR in bacteria, yeast and mammals, MMR genes have not been isolated from higher plants prior to the present invention and no attempts to adjust the plant MMR to plant breeding needs have been reported.

SUMMARY OF THE INVENTION

According to a first embodiment of the invention, there is provided an isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide functionally involved in the DNA mismatch repair system of a plant. In one form of this embodiment, the invention provides an isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human. More particularly, the invention provides polynucleotide sequences encoding polypeptides which are homologous to the mismatch repair polypeptides MSH3 and MSH6 of *Saccharomyces cerevisiae*. Still more particularly, the invention provides the coding sequences of the genes *AtMSH3* and *AtMSH6* of *Arabidopsis thaliana*, as defined hereinbelow, and polynucleotide sequences encoding polypeptides which are homologous to polypeptides encoded by *AtMSH3* and *AtMSH6*.

According to a second embodiment of the invention, there is provided an isolated and purified polypeptide functionally involved in the DNA mismatch repair system of a plant, for example a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human such as a polypeptide encoded by the genes *AtMSH3* or *AtMSH6* of *Arabidopsis thaliana*, as defined hereinbelow.

According to a third embodiment of the invention, there is provided an isolated and purified DNA molecule comprising a polynucleotide sequence selected from the group consisting of (i) a sequence encoding a polynucleotide which is capable of interfering with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human and thereby disabling said plant polynucleotide sequence; and (ii) a sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant.

According to a fourth embodiment of the invention there is provided a chimeric gene comprising a DNA sequence selected from the group consisting of (i) a sequence encoding a polynucleotide which is capable of interfering with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human and thereby disabling said plant polynucleotide sequence, and (ii) a sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant: together with at least one regulation element capable of functioning in a plant cell. Examples of such regulation elements include constitutive, inducible, tissue type specific and cell type specific promoters such as 35S, NOS, PR1a, AoPR1 and DMC1. Typically, a chimeric gene of the fourth embodiment will also include at least one terminator sequence, more typically exactly one terminator sequence.

In the third and fourth embodiments, said interference, by said polynucleotide sequence, with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair peptide of a yeast or a human typically occurs by hybridisation or by co-suppression.

According to a fifth embodiment of the invention there is provided a plasmid or vector comprising a chimeric gene of the fourth embodiment. A vector of the fifth embodiment may be, for example, a viral vector or a bacterial vector.

According to a sixth embodiment of the invention, there is provided a plant cell stably transformed, transfected or electroporated with a plasmid or vector of the fifth embodiment.

According to seventh embodiment of the invention, there is provided a plant comprising a cell of the sixth embodiment.

According to an eighth embodiment of the invention, there is provided a process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising

transforming or transfecting said plant cell with a DNA sequence of the third embodiment or a chimeric gene of the fourth embodiment or a plasmid or vector of the fifth embodiment, and causing said DNA sequence to express said polynucleotide or said polypeptide.

According to a ninth embodiment of the invention, there is provided a process for increasing genetic variation in a plant comprising obtaining a hybrid plant from a first plant and a second plant, or cells thereof, said first and second plants being genetically different; altering the mismatch repair system in said hybrid plant; permitting said hybrid plant to self-fertilise and produce offspring plants; and screening said offspring plants for plants in which homeologous recombination has occurred. For example, homeologous recombination may be evidenced by new genetic linkage of a desired characteristic trait or of a gene which contributes to a desired characteristic trait.

According to a tenth embodiment of the invention there is provided a process for obtaining a plant having a desired characteristic, comprising altering the mismatch repair system in a plant, cell or plurality of cells of a plant which does not have said desired characteristic, permitting mutations to persist in said cells to produce mutated plant cells, deriving plants from said mutated plant cells, and screening said plants for a plant having said desired characteristic.

In a preferred form of the ninth and tenth embodiments of the invention, the step of altering the mismatch repair system comprises introducing into said hybrid plant, plant, cell or cells a chimeric gene of the fourth embodiment and permitting the chimeric gene to express a polynucleotide which is capable of interfering with the expression of a plant polynucleotide sequence in a mismatch repair gene of the hybrid plant, plant, cell or cells, or a polypeptide capable of disrupting the DNA mismatch repair system of the hybrid plant or cells.

In other embodiments, the invention provides (a) an oligonucleotide capable of hybridising at 45°C under standard PCR conditions to a DNA molecule of the first embodiment; (b) an oligonucleotide capable of hybridising at 45°C under standard PCR conditions to the DNA of SEQ ID NO: 18 and (c) an oligonucleotide capable of hybridising at 45°C under standard PCR conditions to the DNA of SEQ ID NO:30; with the proviso that the oligonucleotide of (a), (b) and (c) is other than SEQ ID NO:1 or SEQ ID NO:2.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 provides a diagrammatic representation of the primer sequences used to isolate *AtMSH3*.

Figure 2 is a plasmid map of clone 52, showing restriction enzyme cleavage sites in the 5' half of the full-length cDNA for *AtMSH3*.

Figure 3 is a plasmid map of clone 13, showing restriction enzyme cleavage sites in the 3' half of the full-length cDNA for *AtMSH3*.

Figure 4 is a sequence listing of the coding sequence of *AtMSH3*, together with a deduced sequence of the encoded polypeptide.

Figure 5 is a protein alignment of yeast (*Saccharomyces cerevisiae*) and *Arabidopsis thaliana* MSH3 protein.

Figure 6 provides a diagrammatic representation of the primer sequences used to isolate *AtMSH6*.

Figure 7 is a plasmid map of clone 43, showing restriction enzyme cleavage sites in the 5' half of the full-length cDNA for *AtMSH6*.

Figure 8 is a plasmid map of clone 62, showing restriction enzyme cleavage sites in the 3' half of the full-length cDNA for *AtMSH6*.

Figure 9 is a sequence listing of the coding sequence of *AtMSH6*, together with a deduced sequence of the encoded polypeptide.

Figure 10 is a protein alignment of yeast (*Saccharomyces cerevisiae*) and *Arabidopsis thaliana* MSH6 protein.

Figure 11 is a genomic sequence listing of *AtMSH6*.

Figure 12 is a plasmid map of plasmid pPF13.

Figure 13 is a plasmid map of plasmid pPF14.

Figure 14 is a plasmid map of plasmid pCW186.

Figure 15 is a plasmid map of plasmid pCW187.

Figure 16 is a plasmid map of plasmid pPF66.

Figure 17 is a plasmid map of plasmid pPF57.

Figure 18 is a diagrammatic representation of an antisense gene construction for use in homeologous meiotic recombination.

Figure 19 is a plasmid map of plasmid p3243.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the inventors' discovery that there exist in higher plants genes which are homologous to MMR genes in *E. coli*, and to MMR genes in yeasts and humans.

Thus, the inventors have identified genes, herein designated *AtMSH3* and *AtMSH6*, of the plant *Arabidopsis thaliana* which encode the proteins AtMSH3 and AtMSH6. These plant proteins are homologous to yMSH3 and yMSH6, respectively. The present inventors have isolated cDNAs encoding the proteins AtMSH3 and AtMSH6 and have isolated the complete gene encoding AtMSH6. Given the teaching herein, other genes (for example AtMSH2, and genes of other plants) may be obtained which are involved in DNA mismatch repair in plants, including other genes which encode polypeptides homologous to MMR proteins of yeasts or humans, such as genes which encode

polypeptides homologous to yeast MSH2, MLH1 or PMS2, or to human MLH1, PMS1 or PMS2. For example, given the teaching herein, genes of members of the *Brassicaceae* family or of other unrelated families, for example the *Poaceae*, the *Solanaceae*, the *Asteraceae*, the *Malvaceae*, the *Fabaceae*, the *Linaceae*, the *Canabinaceae*, the *Dauaceae* and the *Cucurbitaceae* family, and which encode polypeptides homologous to MMR proteins of yeasts or humans may be obtained.

Examples of plants whose genes encoding polypeptides homologous to MMR proteins of yeasts or humans may be obtained given the teaching herein include maize, wheat, oats, barley, rice, tomato, potato, tobacco, capsicum, sunflower, lettuce, artichoke, safflower, cotton, okra, beans of many kinds including soybean, peas, melon, squash, cucumber, oilseed rape, broccoli, cauliflower, cabbage, flax, hemp, hops and carrot.

Within the meaning of the present invention, a first polypeptide is defined as homologous to a second polypeptide if the amino acid sequence of the first polypeptide exhibits a similarity of at least 50% on the polypeptide level to the amino acid sequence of the second polypeptide.

A procedure which may be followed to obtain genes *AtMSH3* and *AtMSH6* is described in Example 1. Essentially the same technique may be applied to obtain other mismatch repair genes of *Arabidopsis thaliana*, and essentially the same technique as exemplified herein may be applied to cDNA obtained by reverse transcription of RNA from other plants. Alternatively, given the sequence information disclosed herein, other degenerate oligonucleotide primers, especially oligonucleotides of the invention which are capable of hybridising at 45°C under standard PCR conditions (such as the conditions described in Example 1 using primers UPMU and DOMU) to *AtMSH3* and/or *AtMSH6* may be designed and obtained for use in isolating sequences of plant mismatch repair genes which are homologous to *AtMSH3* or *AtMSH6*, from other plants. Similarly, oligonucleotides of the invention which are capable of hybridising at 45°C under standard PCR conditions to plant mismatch repair genes of plants other than *Arabidopsis thaliana* also fall within the scope of the present invention and may be utilised to obtain mismatch repair genes of still other plants. Typically, such oligonucleotides are capable of hybridising at 45°C under standard PCR conditions to a DNA molecule which encodes a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or a human. The temperature at which oligonucleotides of the invention hybridise to *AtMSH3* and/or *AtMSH6*, or to plant mismatch repair genes of plants other than *Arabidopsis thaliana*, or to DNA molecules which encode polypeptides which are homologous to a mismatch repair polypeptide of a yeast or a human may be higher than 45°C, for example at least 50°C, or at least 55°C, or at least 60°C or as high as 65°C.

The successful gene isolation disclosed herein demonstrates for the first time the existence of MMR in higher plants and indicates the presence of other plant MMR genes. For example, genes encoding the plant homologs of MSH1, MSH2, MSH4, MSH5, PMS1, PMS2 and MLH1 may be identified given the teaching herein. Such genes, as well as those specifically described herein, separately or in combination, are useful in manipulating the plant MMR for plant breeding purposes. Thus, for example, the plant MMR may be altered by including in a plant cell a polynucleotide sequence as defined herein above with reference to the third embodiment of the invention, and causing the polynucleotide sequence to express either a polynucleotide which disables a plant MMR gene, or a polypeptide which disrupts the plant's MMR system.

The DNA molecule of the third embodiment of the invention includes a polynucleotide sequence (herein referred to as a MMR altering gene) which may for example encode sense, antisense or ribozyme molecules characterised by sufficient base sequence similarity or complementarity to the gene to be altered to permit the antisense or ribozyme molecule to hybridise with the plant MMR gene in vivo or to permit the sense molecule to participate in co-suppression. Alternatively, the MMR altering gene may encode a protein or proteins which interfere with the activity of a plant MMR protein and thus disrupt the plant's MMR system. For example, such encoded proteins may be antibodies or other proteins capable of interfering with MMR protein function, such as by complexing with a protein functionally involved in plant MMR thereby disrupting the MMR of the plant. An example of such a protein is the MSH3 protein of *Arabidopsis thaliana* described herein or a protein of another plant which is homologous to the MSH3 protein of *A. thaliana*. For instance, overexpression of MSH3 in a plant cell causes MSH2 present in the cell to be substantially completely complexed, disrupting the mismatch repair mechanism or mechanisms in the cell which are functionally dependent on the presence of a complex of MSH2 with MSH6. Similarly, mismatch repair mechanisms which depend on the presence of a complex of MSH2 and MSH3 may be disrupted by the overexpression of MSH6.

A chimeric gene of the fourth embodiment, incorporating a MMR altering gene, may be prepared by methods which are known in the art. Similarly, the MMR altering gene may be introduced into a plant cell, regenerating tissue or whole plant by techniques known in the art as being suitable for plant transformation, or by crossing. Known transformation techniques include *Agrobacterium tumefaciens* or *A. rhizogenes* mediated gene transfer, ballistic and chemical methods, and electroporation of protoplasts.

The MMR altering gene or genes are typically expressed from suitable promoters. Suitable promoters may direct constitutive expression, such as the 35S or the *NOS* promoter. Usually, however, the promoter will direct either inducible or tissue specific (e.g. callus; embryonic tissue; etc.), cell type specific (e.g. protoplasts; meiocytes, etc.) or developmental (e.g. embryo) expression of the altering gene or genes, in order for the

MMR system to function in tissue types or cell types, or at developmental stages of the plant, in which it is not desirable for the MMR system to be altered. Using such promoters, therefore, the activity of a MMR altering gene may be limited to a specific stage during plant development or it may be altered by controlling conditions external to the plant, and the deleterious effects of a permanently disabled or altered DNA mismatch repair system in a plant may be avoided. Examples of suitable promoters which are not constitutive are known in the art and include inducible promoters such as *PR*1a (reviewed by Gatz, 1997, Annual Rev. Plant Phys. Plant Mol. Biol. 48: 89), tissue specific promoters such as *AoPR1* (Sabahattin et al., 1993, Biotechnology 11: 218), and cell-type specific promoters such as *DMC*1.

A chimeric gene in accordance with the invention may further be physically linked to one or more selection markers such as genes which confer phenotypic traits such as herbicide resistance, antibiotic resistance or disease resistance, or which confer some other recognisable trait such as male sterility, male fertility, grain size, colour, growth rate, flowering time, ripening time, etc.

The process of the tenth embodiment of the invention provides, for example, a process for generating intraspecies genetic variation by altering the mismatch repair system in a plant cell, in regenerating plant tissue or in a whole plant. The plant cell, regenerating tissue or whole plant includes and expresses one or more MMR altering genes which are capable of altering mismatch repair in the plant cell, regenerating tissue or whole plant. Alteration of MMR may be achieved, for example, by inactivating the genes encoding plant MSH3 and/or plant MSH6. It is preferred to inactivate the plant MSH3 and MSH6 encoding genes at the same time and in the same plant cell, regenerating tissue or whole plant. Typically in this preferred form of the invention inactivation of either plant MSH3 or MSH6 alone is insufficient to substantially alter the plant's mismatch repair system and only when both MSH3 and MSH6 are inactivated simultaneously is the plant's mismatch repair system sufficiently altered to prevent the MMR system from recognising base pair mismatches, base insertions or deletions as a result of DNA replication errors, DNA damage, or oligonucleotide induced site-specific mutagenesis. However, in some applications of the invention, inactivation of only one gene may also be used to cause genomic instability or increase the efficiency of site-specific mutagenesis.

If desired, the MMR altering gene or genes may later be rendered non-functional or ineffective, or may be removed from the genome of the plant cell, regenerating tissue or whole plant in order to restore mismatch repair in the plant cell, regenerating tissue or whole plant. The MMR altering gene or genes may be inactivated by means of known gene inactivation tools, such as ribozymes, or may be removed from the genome using gene elimination systems known in the art, such as *CRE/LOX*. It is preferred to render two genes, whose gene products combine to incapacitate MMR, ineffective by separating

the altering genes through segregation. Therefore, in a preferred embodiment of the invention a first plant cell or plant is generated in which only plant *MSH3* is incapacitated, and a second plant cell or plant is generated in which only plant *MSH6* is incapacitated. The combination of both genomes, for example by crossing, then produces significant MMR deficiency in those cells or plants which have inherited both altering genes. If the altering genes are expressed from unlinked loci, gene segregation restores MMR activity in the progeny of the cells or plants.

In a process of the ninth embodiment of this invention, homeologous recombination is enhanced between different genomes, chromosomes or genes in plant cells or plants by altering MMR in said plant cells or plants. Such genomes, chromosomes or genes are characterised in that they originate from different plant families, genera, species, subspecies, plant varieties or lines. Hybrid plant cells or hybrid plants may be produced by crossing, by cell fusion or by other techniques known in the art. These plant cells or plants are further characterised by expressing one or more genes that are capable of altering mismatch repair in the plant cell or plants.

In the process of the ninth embodiment, the homeologous recombination is typically for the purpose of introducing a desired characteristic in the hybrid plant. In this typical application of the process of the ninth embodiment, and in the process of the tenth embodiment the desired characteristic may be any characteristic which is of value to the plant breeder. Examples of such characteristics are well known in the art and include altered composition or quality of leaf or seed derived storage products (e.g. oil, starch, protein), altered composition or quality of cell walls (e.g. decrease in lignin content), altered growth rate, prolonged flowering, increased plant yield or grain yield, altered plant morphology, resistence to pathogens, tolerance to or improved performance under environmental stresses of various kinds, etc.

In a preferred form of the tenth embodiment, an MMR altering gene is co-introduced along with the homeologous genome, chromosome or gene of another plant cell or plant into an MMR proficient plant cell or MMR proficient plant to produce a hybrid plant cell or hybrid plant in which homeologous recombination can occur. Suitably, the MMR proficient plant cell or MMR proficient plant may also include an MMR altering gene. For example a gene capable of inactivating plant MSH3 may be co-introduced along with the homeologous genome, chromosome or gene of another plant cell or plant into an MMR proficient plant cell or MMR proficient plant in which MSH6 is inactivated. A resultant hybrid plant in which homeologous recombination occurs will include both the MSH3 and MSH6 altering genes and its MMR system will therefore be inactivated.

In this form of the invention, if hybrid plants are to be produced by crossing, the MMR altering gene preferably originates from the male parent, thus ensuring that the

MMR altering gene is always introduced and is not present in the recipient cell. That is, the MMR of the recipient cell, prior to introduction of the MMR altering gene, is typically proficient. Alternatively, if an MMR altering gene is present in a recipient cell it may be ineffective or inefficient on its own, or it may be linked to an inducible or tissue specific or cell type specific promoter which only renders the MMR altering gene active under limited conditions.

Thus, in a preferred form of the process of the ninth embodiment, the MMR system of the hybrid plant is initially unaltered. In this form of the process, the step of altering the mismatch repair system may comprise introducing into the hybrid plant, or cells thereof, a MMR altering gene, such as by *Agrobacterium tumefaciens* or *A. rhizogenes* mediated gene transfer, ballistic and chemical methods, and electroporation of protoplasts.

The MMR altering gene or genes are typically expressed from suitable promoters, as described above. Preferably, the promoter is transcriptionally active in mitotically and meiotically active tissue and/or cells to ensure MMR alteration after chromosome pairing at mitosis and meiosis, respectively. The preferred timing for MMR alteration is at meiosis, because recombinant genomes, chromosomes or genes are directly transmitted to the progeny. A suitable meiocyte specific promoter is for example the *DMC*1 promoter from *Arabidopsis thaliana* ssp. *Ler*. (Klimyuk and Jones, 1997, Plant J. 11, 1-14). However, mitotic homeologous recombination is also a desirable outcome as somatic recombination events can be transmitted to offspring due to the totipotency of plant cells and the lack of predetermined germ cells in plants.

If desired, the MMR altering gene or genes may later be rendered non-functional or ineffective, or may be removed from the hybrid plant or hybrid plant cells, in order to restore mismatch repair in the hybrid plant or hybrid plant cells. The MMR altering gene or genes may be inactivated by means of known gene inactivation tools as described herein above.

EXAMPLES

Example 1. Cloning of the *AtMSH3* and *AtMSH6* coding sequences

Isolation of partial *AtMSH3* and *AtMSH6* consensus sequences

Degenerate oligonucleotides UPMU (SEQ ID NO:1) and DOMU (SEQ ID NO:2)

UPMU CTGGATCCACIGGICCIAA(C/T)ATG

DOMU CTGGATCC(A/G)TA(A/G)TGIGTI(A/G)C(A/G)AA

were used to isolate *AtMSH3* and *AtMSH6* sequences by PCR amplification.

Primers UPMU and DOMU correspond to conserved amino acid sequences of the proteins MutS (*E. coli* and *S. typhimurium*), HexA (*S. pneumoniae*), Rep1 (mouse) and Duc1 (human). The conserved regions to which they are targeted are TGPNM for UPMU (amino acid positions 852-856 for AtMSH6 and 816-820 for AtMSH3) FATHY or FVTHY

for DOMU (amino acid positions 964-968 for AtMSH6 and 928-932 for AtMSH3, respectively.) These primers have been used to isolate MSH2 and MSH1 from yeast (Reenan and Kolodner, Genetics 132: 963-973 (1992)) and MSH2 from *Xenopus* and mouse (Varlet et al., Nuc. Acids Res. 22:5723-5728 (1994)).

Template single strand cDNA was produced by reverse transcription of 2 μg total RNA from a cell suspension culture of *Arabidopsis thaliana* ecotype Columbia (Axelos et al. 1989, Mol. Gen. Genetics 219: 106-112). The PCR reaction was performed under the following conditions in a final volume of 100μl: 0.2mM dNTP, 1μM each primer, 1XPCR buffer, 1u *Taq* DNA polymerase (Appligene) in the presence of template cDNA. PCR parameters were 5 minutes at 94°C, followed by 30 cycles of 40 seconds at 95°C, 90 seconds at 45°C, 1 minute at 72°C. The amplification products were cloned into pGEM-T vector (Promega) and sequenced. Two different clones were isolated, S5 (350bp) was homologous to *MSH3*, S8 (327bp) was homologous to *MSH6*. Complete cDNA sequences were then isolated according to the Marathon cDNA amplification kit procedure (Clontech). In summary, this procedure involves producing double stranded cDNA by reverse transcription of 2μg polyA+ RNA from the cell suspension culture of *Arabidopsis*. Adaptors are ligated on each side of the cDNA. The ligated cDNA is used as a template for 5' and 3' RACE PCR reactions in the presence of primers that are specific for the adaptor on one side (AP1 and AP2), and specific for the targeted gene on the other side. A 5' and a 3' fragment that overlap are thus produced for each gene. The complete gene coding sequence can be reconstituted taking advantage of a unique restriction site, if available, in the overlapping region. Specific details of this procedure as it was used to isolate *AtMSH3* and *AtMSH6* coding regions, are as follows.

Isolation of *AtMSH3* complete coding sequence

From the sequence of clone S5, primer 636 (SEQ ID NO:3) was designed:

636 TGCTAGTGCCTCTTGCAAGCTCAT.

Primer AP1 (SEQ ID NO:4) is complementary to a portion of an adaptor sequence which had been ligated to the 5' and 3' ends of *Arabidopsis* cDNA:

AP1 CCATCCTAATACGACTCACTATAGGGC.

PCR performed on the ligated cDNA with primers 636 and AP1 for the 5' RACE PCR was followed by a second round of amplification with the nested primers AP2 (SEQ ID NO:5) and S525 (SEQ ID NO:6)

AP2 ACTCACTATAGGGCTCGAGCGGC

S525 AGGTTCTGATTATGTGTGACGCTTTACTTA

(the latter was also designed to correspond to a part of the sequence of clone S5) and produced a 2720bp DNA fragment. Figure 1 provides a diagrammatic representation of the primer sequences used to isolate *AtMSH3*. Another primer (S51, SEQ ID NO:7)

S51 GGATCGGGTACTGGGTTTTGAGTGTGAGG

was designed closer to the 5' border and permitted the determination of 99bp upstream to the ATG initiation codon. For the 3' RACE PCR, a first PCR reaction was performed with primers AP1 and 635 (SEQ ID NO:8).

635 GCACGTGCTTGATGGTGTTTTCAC

followed by a second round of amplification, using the nested primers AP2 and S523 (SEQ ID NO:9)

S523 TCAGACAGTATCCAGCATGGCAGAAGTA

which produced a DNA fragment of 890bp. Both DNA fragments were subcloned into pGEM-T and sequenced. Since PCR amplification using the Expand Long Template PCR System (Boehringer-Mannheim) produced errors in the sequence, new oligonucleotides were designed to isolate those sequences again by PCR, but with the high fidelity DNA polymerase *Pfu*. PCR with primers 1S5 (SEQ ID NO:10) and S53 (SEQ ID NO:11)

1S5 ATCCCGGGATGGGCAAGCAAAAGCAGCAGACGA

S53 GACAAAGAGCGAAATGAGGCCCCTTGG

amplified the 1244bp fragment clone 52 (SEQ ID NO:12, cloned into pUC18/SmaI). PCR with primers S52 (SEQ ID NO:13) and 2S5 (SEQ ID NO:14)

2S5 ATCCCGGGTCAAAATGAACAAGTTGGTTTTAGTC

S52 GCCACATCTGACTGTTCAAGCCCTCGC

amplified the 2104bp clone 13 (SEQ ID NO:15, cloned into pUC18/SmaI). The complete coding sequence of the *AtMSH3* gene was reconstructed in pUC18 by ligating the 5' half of *AtMSH3* (clone 52) to the 3' half of *AtMSH3* (clone 13) after digesting with *Bam*H1 which has a unique cleavage site in the overlapping region of both clones. This manipulation yielded plasmid pPF26. The *Sma*I fragment from pPF26 contains the complete *AtMSH3* coding sequence. The remaining primers referred to in Figure 1 are as follows:

S51 GGATCGGGTACTGGGTTTTGAGTGTGAGG (SEQ ID NO:16)

S525 AGGTTCTGATTATGTGTGACGCTTTACTTA (SEQ ID NO:17)

Figures 2 and 3 provide plasmid maps of clones 52 and 13 respectively, showing restriction enzyme cleavage sites. The complete *AtMSH3* coding sequence (SEQ ID NO:18) is 3246bp long and is shown in Figure 4 together with the deduced sequence (SEQ ID NO:19) of the encoded polypeptide. *AtMSH3* is clearly homologous to the yeast and mouse *MSH3* genes. A sequence alignment of polypeptides encoded by *AtMSH3* and that encoded by *Saccharomyces cerevisiae MSH3* is set out in Figure 5.

Isolation of the *AtMSH6* complete coding sequence and genomic sequences

The same procedure allowed isolation of the *AtMSH6* cDNA. Figure 6 provides a diagrammatic representation of the primer sequences used to isolate *AtMSH6*. For the 5' RACE PCR, primers 638 (SEQ ID NO:20) and AP1 (SEQ ID NO:4)

638 TCTCTACCAGGTGACGAAAAACCG

allowed the amplification of a 2889 DNA fragment. Primer S81 (SEQ ID NO:21)

S81 CGTCGCCTTTAGCATCCCCTTCCTTCAC

helped define the 142bp upstream to the ATG initiation codon. On the 3' side, RACE PCR was initially performed with primers S823 (SEQ ID NO:22) and AP1 (SEQ ID NO:4).

S823 GCTTGGCGCATCTAATAGAATCATGACAGG

and then with the nested primers 637 (SEQ ID NO:23) and AP2 (SEQ ID NO:5).

637 GACAGCGTCAGTTCTTCAGAATGC

to produce a 774bp DNA fragment. As for *AtMSH3*, those fragments were cloned and sequenced. Re-isolation of the DNA sequence using the high fidelity *Pfu* polymerase and newly designed primers 1S8 (SEQ ID NO:24) and S83 (SEQ ID NO:25) (for the 5' side) led to a 2182 bp DNA fragment identified as clone 43 (SEQ ID NO:26, cloned in pUC18/SmaI), and a 1379bp clone identified as clone 62 (SEQ ID NO:27, also cloned in pUC18/SmaI).

1S8 ATCCCGGGATGCAGCGCCAGAGATCGATTTTGT

2S8 ATCCCGGGTTATTTGGGAACACAGTAAGAGGATT (SEQ ID NO:28)

S82 GCGTTCGATCATCAGCCTCTGTGTTGC (SEQ ID NO:29)

S83 CGCTATCTATGGCTGCTTCGAATTGAG

Figures 7 and 8 provide plasmid maps of clones 43 and 62 respectively, showing restriction enzyme cleavage sites. Clones 43 and 62 were digested by the *XmnI* restriction enzyme for which a unique site is present in their overlapping region and then ligated. The complete *AtMSH6* coding sequence (SEQ ID NO:30) is 3330bp long and is shown in Figure 9 together with the deduced sequence (SEQ ID NO:31) of the encoded polypeptide. *AtMSH6* is clearly homologous to the yeast and mouse *MSH6*genes. A sequence alignment of polypeptides encoded by *AtMSH6* and that encoded by *Saccharomyces cerevisiae MSH6* is set out in Figure 10.

An *AtMSH6* genomic sequence was also isolated from a genomic DNA library constituted after partial *Sau3*AI digestion of DNA from the *Arabidopsis* cell suspension. 8062bp were sequenced that covered the *AtMSH6* gene and show colinearity with the cDNA. 16 introns are found scattered along the gene. The complete genomic sequence (SEQ ID NO:98) is shown in Figure 11.

Example 2. A measure of somatic variation in MMR deficient plants

Constructs

Constructs with antisense *AtMSH3* or antisense *AtMSH6* or both *AtMSH3/AtMSH6* under the control of a single 35S promoter have been inserted into the binary vector pPZP121 (Hajdukiewicz et al., Plant Mol. Biol. 23, 793-799) between the right and left borders of the T-DNA. The pPZP121 plasmid confers chloramphenicol resistance to *Escherichia coli* or *Agrobacterium tumefaciens* bacteria. The *aacC1* gene is carried by the T-DNA and allows selection of transformed plant cells on gentamycin (Hajdukiewicz et al., Plant Mol. Biol. 25, 989-994). For the purpose of expressing antisense constructs, a 35S

promoter/terminator cassette with a polylinker was introduced into pPZP121. The 3' ends of the considered genes have been chosen since this region seems more efficient for antisense inhibition. For *AtMSH3* this corresponds to clone 13 (2104bp), for *AtMSH6* this corresponds to clone 62 (1379bp). Clone 13 comprises 2104bp of the 3' region that were cut off the pUC18 vector by SalI/SstI restriction, blunted with T4 DNA polymerase and ligated into the T4 DNA polymerase blunted *Bam*HI site of pPZP121/35S, creating clone pPF13. The same procedure was followed for the 3' region of *AtMSH*6 clone 62 (1379bp) thus creating plasmid pPF14. For the double constructs, the 3' region (from clone 62) of *AtMSH*6 was introduced ahead of the *AtMSH*3 region into pPF13 creating pCW186 and reciprocally, the 3' region of *AtMSH3* (from clone 13) was introduced ahead of *AtMSH6* into pPF14, creating pCW187.

These constructs were introduced into the Arabidopsis cells (as described below) of wildtype Columbia and of the Columbia tester line.

An alternative strategy to antisense inhibition of *AtMSH6* comes from experiments of Marra et al. (1998. Proc. Natl. Acad. Sci USA 95. *8568-8573)* who show that overexpression of functional *MSH3* results in depletion of MSH6 protein in human cells. This depletion may generate a mismatch repair mutant phenotype.

For the purpose of overexpressing functional *AtMSH3* protein in plant cells, the complete *MSH3* coding region was excised from pPF26 (example 1) by digestion with *Sma*I, and was inserted into the *Sma*I site of pCW164. The resulting construct was named pPF66. It contains a complete *AtMSH3* gene under the control of the *35S* promoter inside the left (LB) and right (RB) border of the T-DNA. This T-DNA also contains the *hpt2* gene for gentamycin selection. Plasmid pPF66 was introduced into Arabidopsis cells as described below. One cell clone was selected which clearly overexpressed the *AtMSH3* gene as shown by Northern analysis. Figures 12-16 provide plasmid maps of plasmids pPF13, pPF14, pCW186, pCW187 and pPF66, respectively.

Construction of tester construct

For the purpose of Forward Mutagenesis Assays, a tester construct was built containing the coding regions for *npt*II, *cod*A, *uid*A. All three genes are driven by the *35S* promoter and are terminated by the *35S* terminator. This construct was obtained by introducing an EcoRI fragment encoding the *cod*A cassette (2.5kb) and a *Hind*III fragment encoding the *uid*A *(GUS)* cassette (2.4kb) into the pPZP111 vector (Hajdukiewicz et al.,1994, Plant Mol Biol 23: 793-799) which already contained the *npt*II expression cassette. This new plasmid was named pPF57. *Npt*II is used to select for transformed plant cells. *GUS* is used to analyse the degree of gene silencing in the construct (i.e. to identify cell lines in which the transgenes are expressed), and *cod*A is used as a marker for forward mutagenesis (described below).

The plasmid map of pPF57 is provided in Figure 17.

Plant cell transformation

The constructs are introduced into *Agrobacterium* by electroporation. Plant cells are then transformed by co-cultivation. A suspension culture of *Arabidopsis thaliana* cells that has been established by Axelos et al. (1992, Plant Physiol. Biochem. 30, 1-6) may be used. One day old freshly subcultured cells are diluted five times into AT medium (Gamborg B5 medium, 30g/l sucrose, 200µg/l NAA). 10µl of saturated *Agrobacterium* containing the transforming T-DNA constructs are added to 10ml diluted cells in a 100ml erlenmeyer. The co-cultivation is agitated slowly (80rpm) for 2 days. The cells are then washed 3 times into AT medium and finally resuspended in the same initial volume (10ml). The culture is agitated for 3 days to allow expression before plating on selection plates (AT/BactoAgar 8g/l+gentamycin 50µg/ml). Transformed individual calli are isolated 3 weeks later.

Tester Strain

The tester construct on plasmid pPF57 was introduced into Arabidopsis cells of wildtype Columbia using the transformation protocol described above. Among 10 candidate transformants, one cell clone was shown (by Southern analysis) to have a unique T-DNA insertion. All three genes were shown to be functional in this cell line as indicated by resistance to kanamycin, blue staining in the presence of X-Glu *(GUS)*, and sensitivity to 5-fluoro-cytosine (*cod*A).

MMR altering genes (described above) were then introduced individually into the tester line and transformed cells are used for analysis of both Microsatellite Instability and Forward Mutagenesis.

Microsatellite analysis

Microsatellites have been described in *Arabidopsis* (Bell and Ecker, 1994, Genomics 19, 137-144). The present Example is based on a study of instability of microsatellites that are polymorphic amongst different ecotypes. DNA is extracted from the transformed calli. Specific primers have been defined that are used to amplify the microsatellite sequence. One of the two primers is previously P^{32} labelled by T4 kinase. In case of a polymorphic variation, new PCR products appear that do not follow the expected pattern of migration on a polyacrylamide gel. This is a commonly observed feature for MMR deficient cells in yeast or mammalian cells.

In particular, the present Example describes a study on microsatellites ca72 (CA_{18}), nga172 (GA_{29}), and ATHGENEA(A_{39}), chosen because they belong to the types predominantly affected in human mismatch repair deficient tumors. The size of these microsatellites is not conserved from one *Arabidopsis* ecotype to the other.

Arabidopsis cells which are transformed with an MMR altering gene (above) and control cells not expressing the MMR altering gene are allowed to form calli. DNA is

rapidly extracted from the calli and is analysed for microsatellite instability as described in detail by Bell and Ecker 1994. Genomics 19, 137-144. In summary, the relevant microsatellite is amplified by PCR using P32 labelled primers. The PCR products are separated on a DNA sequencing gel for size determination. Size differences between microsatellites from transformed and control cells not expressing the MMR altering gene in question indicate microsatellite instability as a result of MMR alteration.

The sequences of primers used for PCR amplification of microsatellites ca72 and nga172 are included in Table 1. PCR amplification of microsatellite ATHGENEA made use of a forward primer containing the sequence

ACCATGCATAGCTTAAACTTCTTG (SEQ ID NO:32)

and of a reverse primer containing the sequence

ACATAACCACAAATAGGGGTGC (SEQ ID NO:33).

The amplification for microsatellite ca72 revealed in Columbia control cells (with respect to the MMR altering gene) a 248 bp long PCR fragment instead of the published length of 124 bp. DNA sequencing verified this fragment as a CA_{18} microsatellite.

Forward mutagenesis assay

Tester cells transformed with antisense *AtMSH3* or antisense *AtMSH6* or both *AtMSH3/AtMSH6* are analysed for the stability of the *cod*A gene. The functional *codA* gene confers to sensitivity to 5-fluoro-cytosine (5FC), whereas a gene inactivating mutation in *cod*A will confer resistance to 5FC. The frequency of resistant cells is therefore a good indicator of somatic variation as a direct result of MMR alteration. Variants resistant to 5FC are first analysed for GUS activity. If GUS is inactive, 5FC resistance is assumed to be due to gene silencing (all three genes are under the *35S* promoter). If GUS is active, 5FC resistance is assumed to be due to forward mutations that have inactivated *cod*A. PCR is then performed on the putative *cod*A mutant genes which is then sequenced to confirm the presence of forward mutations in *cod*A.

Besides *cod*A, other marker genes may also be used for the Forward Mutagenesis Assay such as the *ALS* gene (conferring sensitivity to valine or to sulfonylurea; Hervieu and Vaucheret, 1996, Mol. Gen. Genet. 251 220-224; Mazur et al. 1987, Plant Physiol. *85* 1110-1117).

Example 3. Homeologous meiotic recombination in *Arabidopsis thaliana*

A. Construction of a meiocyte specific gene expression cassette comprising the *DMC*1 promoter and the *NOS* terminator

(i) The *DMC*1 promoter may be used as published by Klimyuk and Jones, 1997, Plant J. 11,1-14). To obtain a more convenient alternative for gene cloning, a 3.3 Kb

long subfragment of the *DMC*1 promoter was obtained by PCR from genomic DNA of *Arabidopsis thaliana* (ssp. Landsberg erecta "*Ler*").

The PCR was done in three rounds:

Round One: A 3.7 Kb long product was obtained using the forward primer DMCIN-A comprising the sequence

GAAGCGATATTGTTCGTG (SEQ ID NO:34)

and the reverse primer DMCIN-B comprising the sequence

AGATTGCGAGAACATTCC (SEQ ID NO:35).

The weak amplification product was then used as template for round two and three.

Round Two: A 3.1 Kb long product comprising the promoter and the 5' untranslated leader was obtained using forward primer DMCIN-1, which contained the sequence

acgcgtcgacTCAGCTATGAGATTACTCGTG (SEQ ID NO:36)

and introduced a *Sal*I cloning site at the 5' end of the promoter fragment, and reverse primer DMCIN-2 which contained the sequence

gctctagaTTTCTCGCTCTAAGACTCTCT (SEQ ID NO:37)

and introduced a *Xba*I site at the 3' end of the PCR fragment.

Round Three: A 0.2 Kb long product comprising the first exon/intron of the *DMC*1 promoter was obtained using forward primer DMCIN-3, which contained the sequence

gctctagaGCTTCTCTTAAGTAAGTGATTGAT (SEQ ID NO:38)

and introduced a *Xba*I site at the 5' end of the PCR fragment, and reverse primer DMCIN-4, containing the sequence

tcccccgggctcgagagatctccatggTTTCTTCAGCTCTATGAATCC (SEQ ID NO:39)

and introduced at the 3' end of the PCR product restriction sites for *Nco*I, *Bgl*II, *Xho*I and *Sma*I.

The products obtained in round Two and Three were digested with *Xba*I and subsequently ligated to reconstitute a 3.3 Kb long *DMC*1 promoter from which the first two in-frame ATG start codons were replaced with a unique restriction site for *Xba*I. This promoter can be cloned between the restriction sites for *Sal*I and *Sma*I of p3264, which contains the *Sac*I-*Eco*RI NOS terminator in pBIN19, to yield the entire expression cassette in pBIN19. This cassette contains the following cloning sites: *Nco*I, *Bgl*II, *Xho*I, *Sma*I and (already present on p3264) *Kpn*I and *Sac*I.

(ii) Another strategy yielded the following convenient *DMC*1 promoter. A 1.8 kb DNA fragment comprising the 3' terminal part of the meiocyte specific *DMC*1 promoter was isolated by PCR from purified genomic DNA of *Arabidopsis thaliana* (ssp. Landsberg erecta "*Ler*"). The forward PCR primer (DMC1a) contained the sequence

acgcgtcgacGAATTCGCAAGTGGGG (SEQ ID NO:40)

and introduced a *Sal*I cloning site at the 5' end of the promoter fragment. The reverse PCR primer (DMC1b) contained the sequence

tccatggagatctcccgggtacCGATTTGCTTCGAGGG (SEQ ID NO:41)

introducing a polylinker region at the 3' end of the promoter fragment. The PCR reaction was carried out with VENT DNA Polymerase (NEB) over 25 cycles using the following cycling protocol: 1 minute at 94°C, 1 minute at 54°C, 2 minutes at 72°C.

The PCR reaction yielded a blunt ended DNA fragment which was digested with restriction enzyme *SalI* and was cloned into the cleavage sites of restriction enzymes *SalI* and *SmaI* in plasmid p2030, a pUC118 derivative containing the *SacI*-*EcoRI* NOS terminator fragment of pBIN121. The cloning yielded plasmid p2031, containing the *DMC*1 promoter-polylinker-NOS terminator expression cassette depicted in Figure 18.

B. Construction of an *MSH*3 antisense gene under the control of the *DMC*1 promoter

A 2.1 kb DNA fragment encoding the carboxyterminal part of AtMSH3 was removed from the polylinker of clone 13 described in Example 1 after (i) digestion with *KpnI*, (ii) blunting of the DNA ends generated by *KpnI* and (iii) digestion with *BamHI*. The isolated fragment was then cloned in antisense orientation downstream of the *DMC*1 promoter in plasmid p2031, which had been digested with restriction enzymes *SmaI* and *BglII*. This cloning yielded plasmid p2033 (Figure 18).

After digestion of p2033 with *EcoRI*, a 4.1 kb DNA fragment was recovered comprising the *DMC*1 promoter, the partial *MSH*3 cDNA in antisense orientation with respect to the promoter and the *NOS* terminator. This fragment was cloned into the *EcoRI* restriction site of plant transformation vector pNOS-Hyg-SCV to yield plasmid p3242 (Figure 18).

C. Construction of a combined *MSH6*/*MSH*3 antisense gene under the control of a single *DMC*1 promoter

A 3.1 kb fragment, encoding in antisense orientation the partial *AtMSH*6 and *AtMSH*3 sequences and the *35S* terminator, was isolated from pCW186 by digestion with *KpnI*. The fragment was treated with *Klenow* enzyme to blunt both ends. It was then cloned into the *SmaI* site of plasmid p3243 (a pNOS-Hyg-SCV derivative, illustrated in Figure 19), which had been opened to delete the region between the *SmaI* sites. Clones containing the fragment in the antisense orientation with respect to the *DMC*1 promoter (described in A(ii) above) were identified by diagnostic digestion with *BamHI*. The selected construct was named p3261.

Another practical way of cloning the double antisense gene is as follows. A 1 kb DNA fragment encoding the carboxyterminal part of AtMSH6 is isolated from clone 62 described in Example 1 after digestion of clone 62 plasmid DNA with *BamHI*, which cleaves in the 5' polylinker region flanking the partial cDNA, and with *EcoRI*, which cleaves within the cDNA. The isolated fragment is treated with *Klenow* enzyme to blunt both its ends and is cloned into the recipient plasmid p2033 or p3242. For the purpose of

cloning, the recipient plasmid may be cleaved with either *Ava*I or *Nco*I and can be blunted with *Klenow* enzyme to produce blunt acceptor ends for fragment cloning. This cloning yields two opposite orientations of cloned fragment DNA with respect to the *DMC*1 promoter. These can be identified by diagnostic digestion with restriction enzymes *Sca*I or *Xmn*I in conjunction with *Sac*I. The selected construct contains the *DMC*1 promoter, the combined partial cDNAs for *AtMSH3* and *AtMSH6* (both cloned in antisense orientation with respect to the *DMC*1 promoter) and the *NOS* terminator. If the recipient plasmid is p2033, the combined antisense gene under control the single *DMC*1 promoter is recovered from the vector after *Eco*RI digestion and is cloned into the *Eco*RI restriction site of pNOS-Hyg-SCV.

D. Construction of a full-length *MSH3* sense gene under control of the *DMC*1 promoter for overexpression of functional MSH3 protein

Overexpression of MSH3 protein was shown in human cells (Marra et al., 1998, Proc. Natl. Acad. Sci. USA 95, 8568-8573) to complex all available *MSH2* protein. This leaves *MSH6* protein without its partner, leading to the degradation of *MSH6* protein and eventually to a mismatch repair phenotype.

This phenomenon is exploited to increase homeologous meiotic recombination in Arabidopsis as an alternative to antisense inhibition of *AtMSH6*. For this purpose the full-length cDNA encoding *AtMSH3* is isolated from plasmid pPF66 by digestion with *Sma*I and is cloned into the *Sma*I site of the *DMC*1 expression cassettes described in A(i).

E. Selection of Recombination markers on homeologous chromosomes of *Arabidopsis thaliana* subspecies *Landsberg erecta* (Ler), *Columbia* (Col) and *C24*, respectively

E(i). Visual recombination markers in *Arabidopsis th.* subspecies *C24*:

Agrobacterium mediated transformation with a T-DNA containing a *35S-GUS* gene, inactivated by insertion of a *35S-Ac* transposable element (Finnegan et al., 1993, Plant Mol. Biol. 22, 625-633), had yielded a *C24* line in which the T-DNA construct was integrated into chromosome 2. Genetic and molecular analysis of this line shows that the *Ac* transposon had excised from its T-DNA locus thereby restoring *GUS* activity, but had re-inserted into the chromosome at a distance of 16.4 cM, where it stayed fixed (due to disablement of *Ac*) within the *chlorina* gene. Insertional inactivation of the *chlorina* gene caused a bleached phenotype in those plants that were homozygous for this mutation. Because of the two linked phenotypic markers, *chlorina3A:Ac* and *GUS*, this *C24* line was used in crosses to wildtype Ler for analysis of meiotic homeologous recombination on chromosome 2 in conjunction with molecular recombination markers.

E(ii). Visual recombination markers in *Arabidopsis th. Ler*:

The Ler line NW1 (obtained from NASC, Nottingham, UK) contains one recessive visual marker per chromosome, i.e. *an-1* on Chr.1, *py-1* on Chr.2, *gl1-1* on Chr.3, *cer2-1*

on Chr.4. and *msl-1* on Chr.5. This line is used in crosses to wildtype *C24* which expresses an MMR altering gene for analysis of meiotic homeologous recombination on chromosomes 1-5 in conjunction with molecular recombination markers listed in Table 1.

Other *Ler* lines from NASC have several visual markers in close proximity to each other on the same chromosome. When these lines are used for hybrid production, analysis of homeologous meiotic recombination may make use entirely of visual recombination markers. Particularly suitable for crossing to *C24* wildtype that is expressing a MMR altering gene are the following *Ler* lines:

NW22: relative markers are *dis1* - (4 cM) - *ga4* - (11 cM) - *th1* on chromosome 1.

NW10: relevant markers are *tz-201* - (5 cM) - *cer3* on chromosome 5.

NW134, relevant markers are *ttg* - (4 cM) - *ga3* on chromosome 5.

NW24 (*abi3*-1) and NW64 (*gl1*-1). When present in the same plant on chromosome 3, *abi3*-1 and *gl1*-1 are 13 cM apart. Since this marker combination is not available from NASC, we have combined these markers by crossing line NW24 to line NW64. The F1 offspring were allowed to self-fertilise and to produce F2 seeds. F2 Plants which carry both markers as homozygous traits on the same chromosome can be identified firstly, by germinating F2 seeds on germination medium containing selective concentrations of abscisic acid, and subsequently, by identifying among the abscisic acid resistant plants those individuals which show the glabra phenotype.

E(iii) Molecular recombination markers in *Col*, *Ler* and *C24*:

The genome of *Arabidopsis thaliana* is interspersed with unique base sequences arranged as simple tandem repeats. Allelic repeats can vary in length between different *Arabidopsis* subspecies and when amplified by PCR yield diagnostic DNA products of different length named Simple Sequence Length Polymorphisms (SSLPs). Many SSLPs have been genetically mapped and have been assigned to unique chromosome locations on the recombinant inbred map (Bell and Ecker, 1994, Genomics 19, 137-144; Lister and Deans lines, Weeds World 4i, May 1997).

In Table 1 are listed 28 mapped and established SSLPs between *Ler* and *Col*. A number of PCR primer pairs are described herein (SEQ ID NO:42 to SEQ ID NO:97) which also yielded SSLPs between *C24* and *Ler* (19 SSLPs) or between *C24* and *Col* (25 SSLPs), respectively. Polymorphic SSLPs can be used as molecular markers in the analysis of homeologous recombination between genomes from these subspecies.

The PCR reactions (25 µL) were carried out over 35 cycles (15 seconds at 94°C, 30 seconds at 55°C and 30 seconds at 72°C), with 0.25 U Taq DNA polymerase and 0.6 µg genomic DNA in reaction buffer containing 2 mM $MgCl_2$. PCR products were separated by agarose gel electrophoresis (4% ultra high resolution agarose) and visualised by ethidiumbromide staining. The results from the PCR experiments are summarised in

Table 1, which also shows the sequence of PCR primers, primer annealing temperature (Tm), PCR product length and chromosome location of SSLP (with respect to the RI map of May 1997, Weeds World 4i).

F. Production of hybrid plants

C24 plants heterozygous for *chlorina3A:Ac/GUS* are crossed as male to emasculated wildtype *Ler* to produce *Ler/C24(chlorina3A, GUS)* hybrid seeds.

Due to the heterozygosity of the *C24* parent, only 50 % of hybrid plants have inherited the *chlorina3A:Ac/GUS* locus. The remaining 50% of hybrid plants are wildtype with respect to *chlorina3A:Ac/GUS*. Since the mutant locus is linked to a kanamycin resistance gene (contained on the same T-DNA as *GUS*) mutant plants can be pre-selected by germinating hybrid seeds on germination medium containing 50 mg/L kanamycin.

Ler plants homozygous for the five chromosome markers are male sterile (*ms1-1*) and are crossed without emasculation to wildtype *C24* to produce *Ler(an-1, py-1, gl1-1, cer2-1, ms1-1)/C24* hybrid seeds.

Other *Ler* plants, which are male fertile, are crossed after emasculation of the female parent to produce *Ler/C24* hybrid seeds.

G. Introduction of *MSH3* and *MSH6/3* antisense genes into Arabidopsis and analysis of meiotic homeologous recombination

(i) Transformation of hybrid plants and analysis of homeologous meiotic recombination

The plant transformation vectors comprising the antisense genes described in (B) and (C) above are introduced into *Agrobacterium tumefaciens* strain *AGL*1 (Lazo et al., 1991, Bio/Technology 9, 963-967) by electroporation. Recombinant *Agrobacterium* clones are selected on LB medium containing 50 mg/L rifampicin and 100 mg/L carbenicillin. Selected clones are used to infect roots of *Arabidopsis* hybrid plants (described in (F) above) using the root transformation protocol of Valvekens et al. (1988, PNAS 85, 5536-5540) except that shoot and root inducing media contain hygromycin (10 mg/L) instead of kanamycin.

Plants regenerated from roots of hybrid plants are genetic clones of root donating plants and therefore are again genetic hybrids of two *Arabidopsis* subspecies described in (F). However, in contrast to the root donating plants, the regenerated hybrid plants also contain the introduced transgene and the co-introduced hygromycin resistance gene with the latter allowing these plants to grow on hygromycin containing culture medium.

Hygromycin resistant plants are then allowed to enter the reproductive phase and to produce gametes by meiotic divisions of microspore and megaspore mothercells. At meiosis, the *DMC*1 promoter is activated and can direct the expression of antisense genes described in (B) and (C) above, leading to decreased *MSH6* and/or *MSH3* gene

expression. This in turn depletes the gamete mothercells of MSH6 and/or MSH3 protein, thus causing alteration of MMR during meiotic divisions and increasing the recombination frequency between homeologous chromosomes.

Transgenic plants are then allowed to self-fertilise and to produce seeds. These seeds (F2 seeds with respect to hybrid production), and the plants derived therefrom, carry the homeologous recombination events which can be identified by using the visual and molecular recombination markers described in (E) above.

In case of homeologous recombination between chromosomes of *Ler* and *C24(chlorina3A:Ac, GUS)*, the analysis concentrates on chromosome 2 by selecting plants showing the visual phenotypic marker *chlorina*. This marker thus serves as a reference point as it indicates that respective chromosomes 2 originate from *C24*. Other markers, such as *GUS* or molecular markers, on chromosome 2 may then be used to identify chromosomal regions which are derived from the *Ler* chromosome as a result of homeologous recombination. F2 plants of control transformants not expressing the antisense gene(s) can be analysed in parallel and the results can be used for comparison to homeologous recombination results obtained in antisense plants.

(ii) Transformation of C24 wildtype, hybrid plant production and analysis of homeologous meiotic recombination

Introduction of MMR altering genes into wildtype *C24* is done using the root transformation protocol as described in G(i) for transformation of hybrid plants. Transformed plants are selected by resistance to either 10 mg/L hygromycin (in case of transformation with T-DNA's derived from pNOS-Hyg-SCV) or to 50 mg/L kanamycin (in case of transformation with T-DNA's derived from pBIN19).

Transgenic plants are then allowed to self-fertilise and to produce seeds (T1 seeds). Segregation of the antibiotic resistance gene in the T1 population then indicates the number of transgene loci. Lines with a single transgene locus (indicated by a 3:1 ratio of resistant:sensitive plants) are selected and are bred to homozygosity. This is done by collecting selfed seeds (T2) from T1 plants and subsequent testing of at least four independent T2 seed populations for segregation of the antibiotic resistance gene. T2 populations which do not segregate the antibiotic resistance gene are assumed to be homozygous for both the resistance gene and the linked MMR altering gene.

C24 plants homozygous for the MMR altering gene are then crossed to *Ler* lines homozygous for recessive visual markers (see E(ii)) to produce *C24/Ler* hybrid plants as described in (F). These F1 hybrids are then allowed to enter the reproductive phase and to produce gametes by meiotic division of microspore and megaspore mothercells. At meiosis, the *DMC* 1 promoter is activated and can direct the expression of antisense or sense genes described in (B), (C) and (D) above, leading to decreased *MSH6* and/or *MSH3* gene expression. This in turn depletes the gamete mothercells of *MSH6* and/or *MSH3*

protein, thus causing alteration of MMR during meiotic divisions and increasing the recombination frequency between the homeologous chromosomes of *C24* and *Ler*. Recombination events are then scored in the F2 generation.

For recombination analysis, the hybrid plants are allowed to self-fertilise and to produce F2 seeds. F2 plants are then preselected for a first visual marker. Since this marker is recessive, its visual presence indicates homozygosity for *Ler* DNA at the relevant locus. Those F2 plants which show this first visual marker are then analysed for the presence or absence of a second visual marker which in the *Ler* parent is closely linked to the first marker. Absence of the second visual marker indicates recombination between the relevant *C24* and *Ler* chromosomes between the first and second marker. The frequency of recombination in transgenic hybrids is compared to the recombination frequency in control hybrids not expressing the MMR altering gene.

Examples of recombination analysis are the following.

The *Ler* line NW22(*dis1*, *ga4* , *th1*) is used for crosses to transformed*C24*.

F2 plants are preselected first for thiamine requirement (*th1*) and then are further analysed for re-appearance of wildtype height (loss of *ga4*) and/or re-appearance of normal trichomes (loss of *dis1*) as a result of recombination.

The *Ler* line NW10(*tz-201*, *cer3*) is used for crosses to transformed*C24*.

F2 plants are then preselected first for thiazole requirement (*tz*) and then are further analysed for re-appearance of normal, i.e. non-shiny stems (loss of *cer3*) as a result of recombination.

The *Ler* line NW134 (*ttg* , *ga3*) is used for crosses to transformed*C24*. F2 plants are first preselected for dwarfish appearance (*ga3*) and are then analysed for re-appearance of trichomes (loss of *ttg*) as a result of recombination.

Ler plants homozygous for *abi3*-1 and *gl1*-1 are used for crosses to transformed*C24*. F2 plants are first preselected for their ability to germinate in the presence of abscisic acid and are then analysed for re-appearance of trichomes on the leaves (loss of *gl1*-1) as a result of recombination.

In the case of homeologous recombination between transformed*C24* and the *Ler* line NW1 (*an-1*, *py-1*, *gl1*-1, *cer2*-1, *ms1*-1), recombination analysis is similar the one described above, except that the second marker is not a visual marker but has to be a molecular marker. This is because the *Ler* parent carries only one visual marker per chromosome.

TABLE 1: SSLP Markers in *Arabidopsis thaliana* Subspecies

Chromosome	RI Map Position	PCR Primer Pair	Primer Sequence	Tm [°C]	length/COL	length/LER	length/C24
I	2.3	ATEAT1 F	GCCACTGCGTGAATGATATG	57.8	172	162	162
		ATEAT1 R	CGAACAGCCAACATTAATTCCC	58.2			
I	9.3	NGA63 F	AACCAAGGCACAGAAGCG	57.3	111	89	120
		NGA63 R	ACCCAAGTGATCGCCACC	59.6			
I	40.1	NGA248 F	TACCGAACCAAAACACAAAGG	56.1	143	129	no amplific.
		NGA248 R	TCTGTATCTCGGTGAATTCTCC	58.2			
I	81.2	NGA128 F	GGTCTGTTGATGTCGTAAGTCG	60.1	180	190	no amplific.
		NGA128 R	ATCTTGAAACCTTTAGGGAGGG	58.2			
I	81.2	NGA280 F	CTGATCTCACGGACAATAGTGC	60.1	105	85	85
		NGA280 R	GGCTCCATAAAAAGTGCACC	57.8			
I	111.4	NGA111 F	CTCCAGTTGGAAGCTAAAGGG	60	128	162	170
		NGA111 R	TGTTTTTTAGGACAAATGGCG	70			
II	ca. 7.5	NGA168 F	CCTTCACATCCAAAACCCAC	57.8	213	217	208
		NGA168 R	GCACATACCCACAACCAGAA	57.8			

II	ca. 48	NGA1126L	CGCTACGCTTTTCGGTAAAG	57.8	191	199	196
		NGA1126R	GCACAGTCCAAGTCACAACC	59.9			
II	62.2	NGA361L	AAAGAGATGAGAATTTGGAC	51.7	114	120	114
		NGA361R	ACATATCAATATATTAAAGTAGC	49.5			
II	73	NGA168 F	TCGTCTACTGCACTGCCG	59.6	151	135	135
		NGA168 R	GAGGACATGTATAGGAGCCTCG	61.9			
II	ca. 77	AthBIO2 L	TGACCTCCTCTTCCATGGAG	59.9	141	209	139
		AthBIO2 R	TTAACAGAAACCCAAAGCTTTC	54.5			
II	ca. 83	AthUBIQUE L	AGGCAAATGTCCATTTCATTG	54.1	146	148	148
		AthUBIQUE R	ACGACATGGCAGATTTCTCC	57.8			
III	3.4	NGA172 F	AGCTGCTTCCTTATAGCGTCC	60	162	136	140
		NGA172 R	CATCCGAATGCCATTGTTC	55.4			
III	12.8	NGA126 F	GAAAAAACGCTACTTTCGTGG	56.1	119	147	no amplific.
		NGA126 R	CAAGAGCAATATCAAGAGCAGC	58.2			
III	17.5	NGA162 F	CATGCAATTTGCATCTGAGG	55.8	107	89	no amplific.
		NGA162 R	CTCTGTCACTCTTTTCCTCTGG	60.1			

III	81.8	NGA6 F	TGGATTTCTTCCTCTCTTCAC	56.1	143	123	143
		NGA6 R	ATGGAGAAGCTTACACTGATC	56.1			
IV	19.8	NGA12 F	AATGTTGTCCTCCCCTCCTC	59.9	247	234	220
		NGA12 R	TGATGCTCTCTGAAACAAGAGC	58.2			
IV	24.1	NGA8 F	GAGGGCAAATCTTTATTTCGG	56.1	154	198	190
		NGA8 R	TGGCTTTCGTTTATAAACATCC	54.5			
IV	102	NGA1107 L	GCGAAAAAACAAAAAAATCCA	50.2	150	140	140
		NGA1107 R	CGACGAATCGACAGAATTAGG	58			
V	11.8	NGA225 F	GAAATCCAAATCCCAGAGAGG	58	119	189	119
		NGA225 R	TCTCCCCACTAGTTTTGTGTCC	60.1			
V	16.7	NGA249 F	TACCGTCAATTTCATCGCC	55.4	125	115	115
		NGA249 R	GGATCCCTAACTGTAAAATCCC	58.2			
V	19.9	CA72 F	AATCCCAGTAACCAAACACACA	56.3	124	110	110
		CA72 R	CCCAGTCTAACCACGACCAC	61.9			
V	20	NGA151 F	GTTTTGGGAAGTTTTGCTGG	55.8	150	120	130
		NGA151 R	CAGTCTAAAAGCGAGAGTATGATG	58.6			

V	24	NGA106 F	GTTATGGAGTTTCTAGGGCACG	60.1	157	123	130
		NGA106 R	TGCCCCATTTTGTTCTTCTC	55.8			
V	37.8	NGA139 F	AGAGCTACCAGATCCGATGG	59.9	174	132	132
		NGA139 R	GGTTTCGTTTCACTATCCAGG	55.8			
V	50	NGA76 F	GGAGAAAATGTCACTCTCCACC	60.1	231	>250	300
		NGA76 R	AGGCATGGGAGACATTTACG	57.8			
V	61.1	ATHSO191 L	CTCCACCAATCATGCAAATG	55.8	148	156	146
		ATHSO191 R	TGATGTTGATGGAGATGGTCA	53.7			
V	81.7	NGA129 F	TCAGGAGGAACTAAAGTGAGGG	60.1	177	179	172
		NGA129 R	CACACTGAAGATGGTCTTGAGG	60.1			

CLAIMS

1. An isolated and purified DNA molecule comprising a polynucleotide sequence encoding a polypeptide functionally involved in the DNA mismatch repair system of a plant.

2. A DNA molecule according to claim 1 wherein said polypeptide is homologous to a mismatch repair polypeptide of a yeast or of a human.

3. A DNA molecule according to claim 1 wherein said polypeptide is homologous to AtMSH3 (SEQ ID NO: 19) or to AtMSH6 (SEQ ID NO: 31).

4. An isolated and purified polypeptide functionally involved in the DNA mismatch repair system of a plant.

5. A polypeptide according to claim 4 which is homologous to a mismatch repair polypeptide of a yeast or of a human.

6. An isolated and purified polypeptide selected from the group consisting of a polypeptide encoded by the gene *AtMSH3* (SEQ ID NO: 18), a polypeptide encoded by the gene *AtMSH6* (SEQ ID NO:30), polypeptides homologous to a polypeptide encoded by the gene *AtMSH3* (SEQ ID NO: 18) and polypeptides homologous to a polypeptide encoded by the gene *AtMSH6* (SEQ ID NO:30).

7. An isolated and purified DNA molecule comprising a polynucleotide sequence selected from the group consisting of (i) a sequence encoding a polynucleotide which is capable of interfering with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human and thereby disabling said plant polynucleotide sequence; and (ii) a sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant.

8. A DNA molecule according to claim 7 comprising a polynucleotide sequence encoding a polynucleotide capable of interfering with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human and thereby disabling said plant polynucleotide sequence.

9. A DNA molecule according to claim 8 wherein said polynucleotide is capable of interfering with the expression of a plant polynucleotide sequence is a sense polynucleotide, an antisense polynucleotide or a ribozyme.

10. A DNA molecule according to claim 7 comprising a polynucleotide sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant.

11. A DNA molecule according to claim 10 wherein said polypeptide is homologous to AtMSH3 (SEQ ID NO: 19) or to AtMSH6 (SEQ ID NO: 31).

12. A DNA molecule according to claim 10 further comprising a regulation element capable of causing overexpression of said polypeptide in a cell of said plant.

13. A chimeric gene comprising:

a DNA sequence selected from the group consisting of (i) a sequence encoding a polynucleotide capable of interfering with the expression of a plant polynucleotide sequence encoding a polypeptide which is homologous to a mismatch repair polypeptide of a yeast or of a human and thereby disabling said plant polynucleotide sequence, and (ii) a sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant; and

at least one regulation element capable of functioning in a plant cell.

14. A chimeric gene according to claim 13 wherein said regulation element is selected from constitutive, inducible, tissue type specific and cell type specific promoters.

15. A chimeric gene according to claim 13 comprising a DNA sequence encoding a polypeptide capable of disrupting the DNA mismatch repair system of a plant, wherein said regulation element is capable of causing overexpression of said polypeptide in a cell of said plant.

16. A chimeric gene according to claim 13 wherein said regulation element is selected from the group consisting of 35S, NOS, PR1a, AoPR1 and DMC1.

17. A plasmid or vector comprising a chimeric gene according to any one of claims 13-16.

18. A plant cell stably transformed, transfected or electroporated with a plasmid or vector according to claim 17.

19. A plant comprising a cell according to claim 18.

20. A plant according to claim 19 selected from plants of the families *Brassicaceae*, *Poaceae*, *Solanaceae*, *Asteraceae*, *Malvaceae*, *Fabaceae*, *Linaceae*, *Canabinaceae*, *Dauaceae* and *Cucurbitaceae*.

21. A process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising transforming or transfecting said plant cell with a DNA molecule according to any one of claims 1-3 or 7-12 and causing said DNA sequence to express said polynucleotide or said polypeptide.

22. A process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising transforming or transfecting said plant cell with a chimeric gene

according to any one of claims 13-16 and causing said DNA sequence to express said polynucleotide or said polypeptide.

23. A process for at least partially inactivating a DNA mismatch repair system of a plant cell, comprising transforming or transfecting said plant cell with a plasmid or vector according to claim 17 and causing said DNA sequence to express said polynucleotide or said polypeptide.

24. A process for increasing genetic variation in a plant comprising obtaining a hybrid plant from a first plant and a second plant, or cells thereof, said first and second plants being genetically different; altering the mismatch repair system in said hybrid plant; permitting said hybrid plant to self-fertilise and produce offspring plants; and screening said offspring plants for plants in which homeologous recombination has occurred.

25. A process according to claim 24 wherein a first gene is incapacitated in said first plant, a second gene is incapacitated in said second plant, and said first and second genes are incapacitated in said hybrid plant thereby altering the mismatch repair system of said hybrid plant.

25. A process according to claim 25 wherein said incapacitation of the mismatch repair system of said hybrid plant is reversible.

26. A process according to claim 24 wherein a new genetic linkage of a desired characteristic trait or of a gene which contributes to a desired characteristic trait is observable in at least one of said offspring plants.

27. A process for obtaining a plant having a desired characteristic, comprising altering the mismatch repair system in a plant, cell or plurality of cells of a plant which does not have said desired characteristic, permitting mutations to persist in said cells to produce mutated plant cells, deriving plants from said mutated plant cells, and screening said plants for a plant having said desired characteristic.

28. A process according to claim 27 wherein said step of altering the mismatch repair system comprises introducing into said hybrid plant, plant, cell or cells a chimeric gene according to claim 13 and permitting the chimeric gene to express a polynucleotide which is capable of interfering with the expression of a plant polynucleotide sequence in a mismatch repair gene of the hybrid plant, plant, cell or cells, or a polypeptide capable of disrupting the DNA mismatch repair system of the hybrid plant, cell or cells.

29. A process according to claim 28 comprising inactivating an MSH3 gene and/or an MSH6 gene of said plant.

30. A process according to claim 28 comprising inactivating an MSH3 gene and an MSH6 gene of said plant.

31. A process according to claim 27 comprising at least partially inactivating the mismatch repair system of said plant in a predetermined cell type or in a predetermined tissue of said plant.

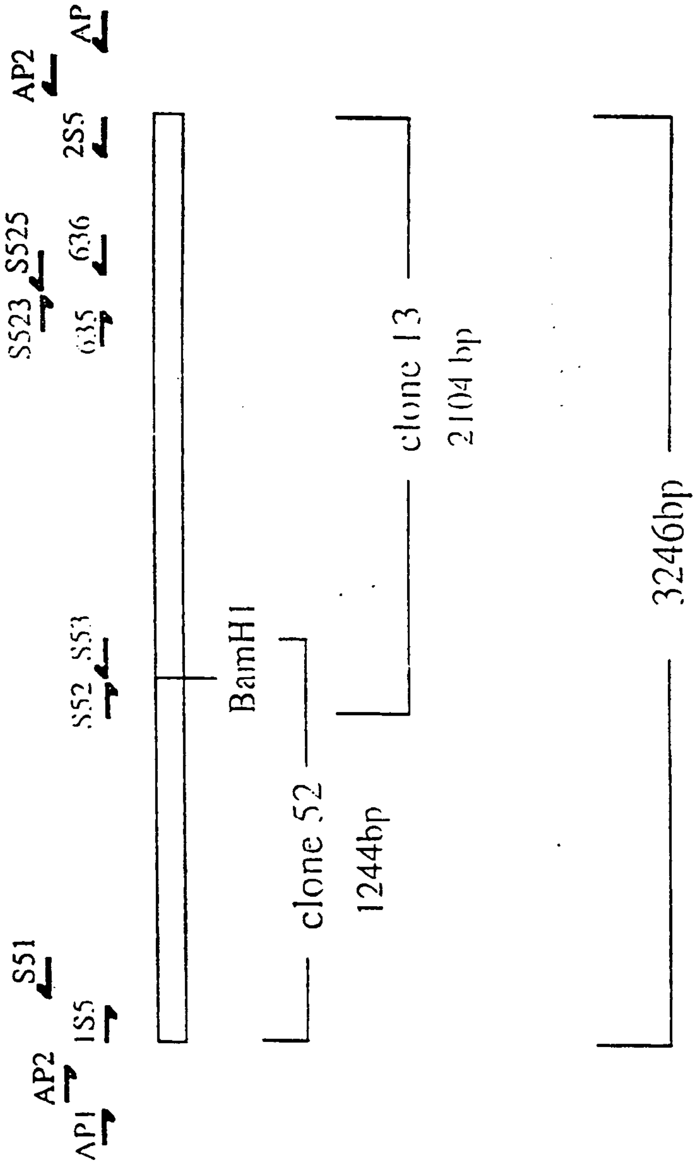
32. A process according to claim 31 further comprising restoring mismatch repair in said cell type or said tissue.

33. An oligonucleotide capable of hybridising at 45°C under standard PCR conditions to a DNA molecule according to claim 1 with the proviso that said oligonucleotide is other than SEQ ID NO:1 or SEQ ID NO:2.

34. An oligonucleotide capable of hybridising at 45°C under standard PCR conditions to the DNA of SEQ ID NO: 18 with the proviso that said oligonucleotide is other than SEQ ID NO:1 or SEQ ID NO:2.

35. An oligonucleotide capable of hybridising at 45°C under standard PCR conditions to the DNA of SEQ ID NO:30 with the proviso that said oligonucleotide is other than SEQ ID NO:1 or SEQ ID NO:2.

Figure 1


AP1
AP2
1S5
S51
S52
S53
BamHI
S523
S525
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636
2S5
AP2
AP1
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1244bp
clone 13
2104 bp
3246bp

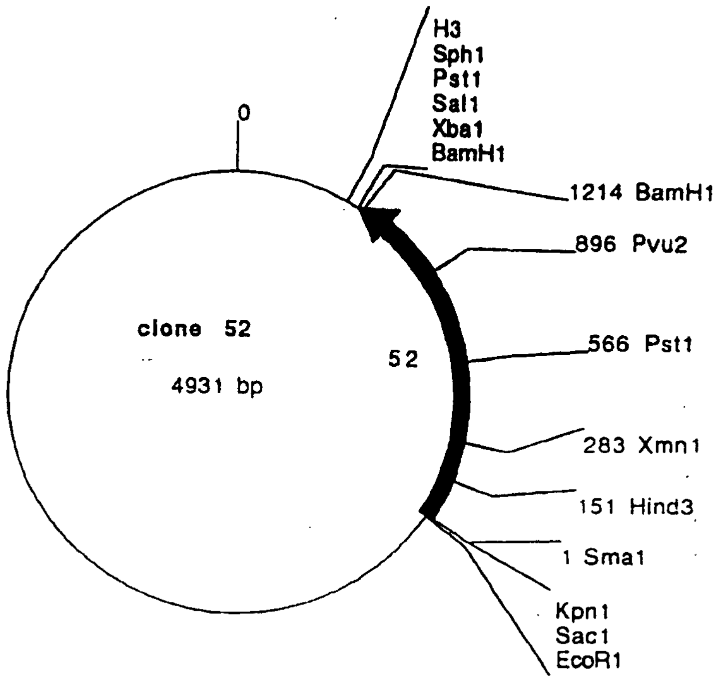

Figure 2

Comments/References: 52= 3' side of S5 (AtMSH3) 1244bp in pUC18/Sma1

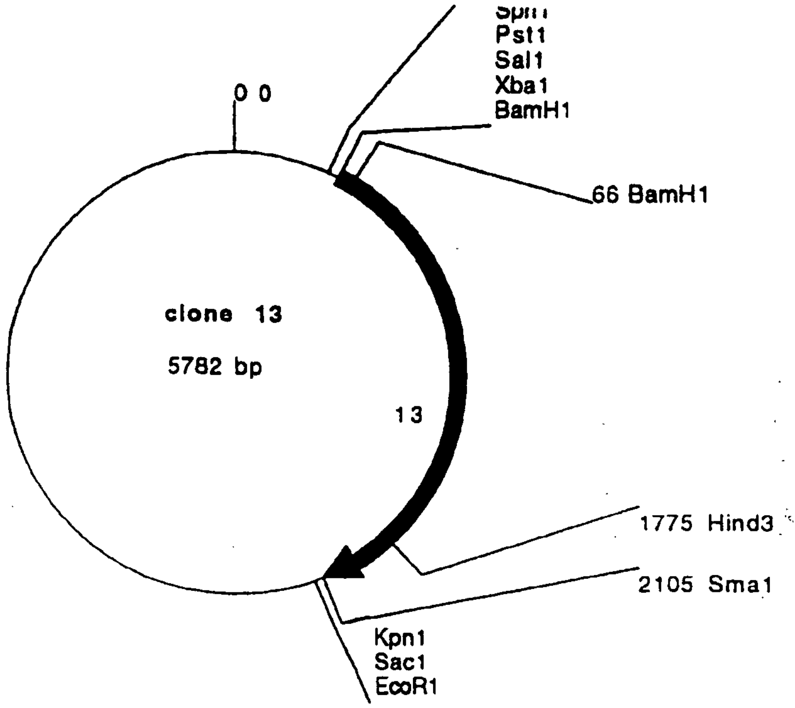

Figure 3

Comments/References: 13 = 3' side of S5 (AtMSH3) 2104bp in pUC18/Sma1

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1    cCTAAGAAAGCGCGCGAAAATTGGCAACCCAAGTTCGCCATAGCCACGACCACGACCTTCCATTTCTCTTAAACGGAGGA   80

81   GATTACGAATAAAGCAATT ATG GGC AAG CAA AAG CAG CAG ACG ATT TCT CGT TTC TTC GCT CCC   144
1                         M   G   K   Q   K   Q   Q   T   I   S   R   F   F   A   P    15

145  AAA CCC AAA TCC CCG ACT CAC GAA CCG AAT CCG GTA GCC GAA TCA TCA ACA CCG CCA CCG   204
16    K   P   K   S   P   T   H   E   P   N   P   V   A   E   S   S   T   P   P   P    35

205  AAG ATA TCC GCC ACT GTA TCC TTC TCT CCT TCC AAG CGT AAG CTT CTC TCC GAC CAC CTC   264
36    K   I   S   A   T   V   S   F   S   P   S   K   R   K   L   L   S   D   H   L    55

265  GCC GCC GCG TCA CCC AAA AAG CCT AAA CTT TCT CCT CAC ACT CAA AAC CCA GTA CCC GAT   324
56    A   A   A   S   P   K   K   P   K   L   S   P   H   T   Q   N   P   V   P   D    75

325  CCC AAT TTA CAC CAA AGA TTT CTC CAG AGA TTT CTG GAA CCC TCG CCG GAG GAA TAT GTT   384
76    P   N   L   H   Q   R   F   L   Q   R   F   L   E   P   S   P   E   E   Y   V    95

385  CCC GAA ACG TCA TCA TCG AGG AAA TAC ACA CCA TTG GAA CAG CAA GTG GTG GAG CTA AAG   444
96    P   E   T   S   S   S   R   K   Y   T   P   L   E   Q   Q   V   V   E   L   K   115

445  AGC AAG TAC CCA GAT GTG GTT TTG ATG GTG GAA GTT GGT TAC AGG TAC AGA TTC TTC GGA   504
116   S   K   Y   P   D   V   V   L   M   V   E   V   G   Y   R   Y   R   F   F   G   135

505  GAA GAC GCG GAG ATC GCA GCA CGC GTG TTG GGT ATT TAC GCT CAT ATG GAT CAC AAT TTC   564
136   E   D   A   E   I   A   A   R   V   L   G   I   Y   A   H   M   D   H   N   F   155

565  ATG ACG GCG AGT GTG CCA ACA TTT CGA TTG AAT TTC CAT GTG AGA AGA CTG GTG AAT GCA   624
156   M   T   A   S   V   P   T   F   R   L   N   F   H   V   R   R   L   V   N   A   175

625  GGA TAC AAG ATT GGT GTA GTG AAG CAG ACT GAA ACT GCA GCC ATT AAG TCC CAT GGT GCA   684
176   G   Y   K   I   G   V   V   K   Q   T   E   T   A   A   I   K   S   H   G   A   195

665  AAC CGG ACC GGC CCT TTT TTC CGG GCA CTG TCG GCG TTG TAT ACC AAA GCC ACG CTT GAA   744
196   N   R   T   G   P   F   F   R   G   L   S   A   L   Y   T   K   A   T   L   E   215

745  GCG GCT GAG GAT ATA AGT GGT GGT TGT GGT GGT GAA GAA GGT TTT GGT TCA CAG AGT AAT   804
216   A   A   E   D   I   S   G   G   C   G   G   E   E   G   F   G   S   Q   S   N   235

805  TTC TTG GTT TGT GTT GTG GAT GAG AGA GTT AAG TCG GAG ACA TTA GGC TGT GGT ATT GAA   864
236   F   L   V   C   V   V   D   E   R   V   K   S   E   T   L   G   C   G   I   E   255

865  ATG AGT TTT GAT GTT AGA GTC GGT GTT GTT GGC GTT GAA ATT TCG ACA GGT GAA GTT GTT   924
256   M   S   F   D   V   R   V   G   V   V   G   V   E   I   S   T   G   E   V   V   275
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Figure 4

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925   TAT GAA GAG TTC AAT GAT AAT TTC ATG AGA AGT GGA TTA GAG GCT GTG ATT TTG AGC TTG   984
276   Y   E   E   F   N   D   N   F   M   R   S   G   L   E   A   V   I   L   S   L     295

985   TCA CCA GCT GAG CTG TTG CTT GGC CAG CCT CTT TCA CAA CAA ACT GAG AAG TTT TTG GTG   1044
296   S   P   A   E   L   L   L   G   Q   P   L   S   Q   Q   T   E   K   F   L   V     315

1045  GCA CAT GCT GGA CCT ACC TCA AAC GTT CGA GTG GAA CGT GCC TCA CTG GAT TGT TTC AGC   1104
316   A   M   A   G   P   T   S   N   V   R   V   E   R   A   S   L   D   C   F   S     335

1105  AAT GGT AAT GCA GTA GAT GAG GTT ATT TCA TTA TGT GAA AAA ATC AGC GCA GGT AAC TTA   1164
336   N   G   N   A   V   D   E   V   I   S   L   C   E   K   I   S   A   G   N   L     355

1165  GAA GAT GAT AAA GAA ATG AAG CTG GAG GCT GCT GAA AAA GGA ATG TCT TGC TTG ACA GTT   1224
356   E   D   D   K   E   M   K   L   E   A   A   E   K   G   M   S   C   L   T   V     375

1225  CAT ACA ATT ATG AAC ATG CCA CAT CTG ACT GTT CAA GCC CTC GCC CTA ACG TTT TGC CAT   1284
376   H   T   I   M   N   M   P   H   L   T   V   Q   A   L   A   L   T   F   C   H     395

1285  CTC AAA CAG TTT GGA TTT GAA AGG ATC CTT TAC CAA GGG GCC TCA TTT CGC TCT TTG TCA   1344
396   L   K   Q   F   G   F   E   R   I   L   Y   Q   G   A   S   F   R   S   L   S     415

1345  AGT AAC ACA GAG ATG ACT CTC TCA GCC AAT ACT CTG CAA CAG TTG GAG GTT GTG AAA AAT   1404
416   S   N   T   E   M   T   L   S   A   N   T   L   Q   Q   L   E   V   V   K   N     435

1405  AAT TCA GAT GGA TCG GAA TCT GGC TCC TTA TTC CAT AAT ATG AAT CAC ACA CTT ACA GTA   1464
436   N   S   D   G   S   E   S   G   S   L   F   H   N   M   N   H   T   L   T   V     455

1465  TAT GCT TCC AGG CTT CTT AGA CAC TGG GTG ACT CAT CCT CTA TGC GAT AGA AAT TTG ATA   1524
456   Y   G   S   R   L   L   R   H   W   V   T   H   P   L   C   D   R   N   L   I     475

1525  TCT GCT CGG CTT GAT GCT GTT TCT GAG ATT TCT GCT TGC ATG GGA TCT CAT AGT TCT TCC   1584
476   S   A   R   L   D   A   V   S   E   I   S   A   C   M   G   S   H   S   S   S     495

1585  CAG CTC AGC AGT GAG TTG GTT GAA GAA GGT TCT GAG AGA GCA ATT GTA TCA CCT GAG TTT   1644
496   Q   L   S   S   E   L   V   E   E   G   S   E   R   A   I   V   S   P   E   F     515

1645  TAT CTC GTG CTC TCC TCA GTC TTG ACA GCT ATG TCT AGA TCA TCT GAT ATT CAA CGT GGA   1704
516   Y   L   V   L   S   S   V   L   T   A   M   S   R   S   S   D   I   Q   R   G     535

1705  ATA ACA AGA ATC TTT CAT CGG ACT GCT AAA GCC ACA GAG TTC ATT GCA GTT ATG GAA GCT   1764
536   I   T   R   I   F   H   R   T   A   K   A   T   E   F   I   A   V   M   E   A     555

1765  ATT TTA CTT GCG GGG AAG CAA ATT CAG CGG CTT GGC ATA AAG CAA GAC TCT GAA ATG AGG   1824
556   I   L   L   A   G   K   Q   I   Q   R   L   G   I   K   Q   D   S   E   M   R     575
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Figure 4 (Continued)

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1825 AGT ATG CAA TCT GCA ACT GTG CGA TCT ACT CTT TTG AGA AAA TTG ATT TCT GTT ATT TCA 1884
576  S   M   Q   S   A   T   V   R   S   T   L   L   R   K   L   I   S   V   I   S   595

1885 TCC CCT GTT GTG GTT GAC AAT GCC GGA AAA CTT CTC TCT GCC CTA AAT AAG GAA GCG GCT 1944
596  S   P   V   V   V   D   N   A   G   K   L   L   S   A   L   N   K   E   A   A   615

1945 GTT CGA GGT GAC TTG CTC GAC ATA CTA ATC ACT TCC AGC GAC CAA TTT CCT GAG CTT GCT 2004
616  V   R   G   D   L   L   D   I   L   I   T   S   S   D   Q   F   P   E   L   A   635

2005 GAA GCT CGC CAA GCA GTT TTA GTC ATC AGG GAA AAG CTG GAT TCC TCG ATA GCT TCA TTT 2064
636  E   A   R   Q   A   V   L   V   I   R   E   K   L   D   S   S   I   A   S   F   655

2065 CGC AAG AAG CTC GCT ATT CGA AAT TTG GAA TTT CTT CAA GTG TCG GGG ATC ACA CAT TTG 2124
656  R   K   K   L   A   I   R   N   L   E   F   L   Q   V   S   G   I   T   H   L   675

2125 ATA GAG CTG CCC GTT GAT TCC AAG GTC CCT ATG AAT TGG GTG AAA GTA AAT AGC ACC AAG 2184
676  I   E   L   P   V   D   S   K   V   P   H   N   W   V   K   V   N   S   T   K   695

2185 AAG ACT ATT CGA TAT CAT CCC CCA GAA ATA GTA GCT GGC TTG GAT GAG CTA GCT CTA GCA 2244
696  K   T   I   R   Y   H   P   P   E   I   V   A   G   L   D   E   L   A   L   A   715

2245 ACT GAA CAT CTT GCC ATT GTG AAC CGA GCT TCG TGG GAT AGT TTC CTC AAG AGT TTC AGT 2304
716  T   E   H   L   A   I   V   N   R   A   S   W   D   S   F   L   K   S   F   S   735

2305 AGA TAC TAC ACA GAT TTT AAG GCT GCC GTT CAA GCT CTT GCT GCA CTG GAC TGT TTG CAC 2364
736  R   Y   Y   T   D   F   K   A   A   V   Q   A   L   A   A   L   D   C   L   H   755

2365 TCC CTT TCA ACT CTA TCT AGA AAC AAG AAC TAT GTC CGT CCC GAG TTT GTG GAT GAC TGT 2424
756  S   L   S   T   L   S   R   N   K   N   Y   V   R   P   E   F   V   D   D   C   775

2425 GAA CCA GTT GAG ATA AAC ATA CAG TCT GGT CGT CAT CCT GTA CTG GAG ACT ATA TTA CAA 2484
776  E   P   V   E   I   N   I   Q   S   G   R   H   P   V   L   E   T   I   L   Q   795

2485 GAT AAC TTC GTC CCA AAT GAC ACA ATT TTG CAT GCA GAA GGG GAA TAT TGC CAA ATT ATC 2544
796  D   N   F   V   P   N   D   T   I   L   H   A   E   G   E   Y   C   Q   I   I   815

2545 ACC GGA CCT AAC ATG GGA GGA AAG AGC TGC TAT ATC CGT CAA GTT GCT TTA ATT TCC ATA 2604
816  T   G   P   N   M   G   G   K   S   C   Y   I   R   Q   V   A   L   I   S   I   835

2605 ATG GCT CAG GTT GGT TCC TTT GTA CCA GCG TCA TTC GCC AAG CTG CAC GTG CTT GAT GGT 2664
836  M   A   Q   V   G   S   F   V   P   A   S   F   A   K   L   H   V   L   D   G   855

2665 GTT TTC ACT CGG ATG GGT GCT TCA GAC AGT ATC CAG CAT GGC AGA AGT ACC TTT CTA GAA 2724
856  V   F   T   R   M   G   A   S   D   S   I   Q   H   G   R   S   T   F   L   E   875
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Figure 4 (Continued)

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2725  GAA TTA AGT GAA GCG TCA CAC ATA ATC AGA ACC TGT TCT TCT CGT TCG CTT GTT ATA TTA  2784
876   E   L   S   E   A   S   H   I   I   R   T   C   S   S   R   S   L   V   I   L    895

2785  GAT GAG CTT GGA AGA GGC ACT AGC ACA CAC GAC GGT GTA GCC ATT GCC TAT GCA ACA TTA  2844
896   D   E   L   G   R   G   T   S   T   H   D   G   V   A   I   A   Y   A   T   L    915

2845  CAG CAT CTC CTA GCA GAA AAG AGA TGT TTG GTT CTT TTT GTC ACG CAT TAC CCT GAA ATA  2904
916   Q   H   L   L   A   E   K   R   C   L   V   L   F   V   T   H   Y   P   E   I    935

2905  GCT GAG ATC AGT AAC GGA TTC CCA GGT TCT GTT GGG ACA TAC CAT GTC TCG TAT CTG ACA  2964
936   A   E   I   S   N   G   F   P   G   S   V   G   T   Y   H   V   S   Y   L   T    955

2965  TTG CAG AAG GAT AAA GGC AGT TAT GAT CAT GAT GAT GTG ACC TAC CTA TAT AAG CTT GTG  3024
956   L   Q   K   D   K   G   S   Y   D   H   D   D   V   T   Y   L   Y   K   L   V    975

3025  CGT GGT CTT TGC AGC AGG AGC TTT GGT TTT AAG GTT GCT CAG CTT GCC CAG ATA CCT CCA  3084
976   R   G   L   C   S   R   S   F   G   F   K   V   A   Q   L   A   Q   I   P   P    995

3085  TCA TGT ATA CGT CGA GCC ATT TCA ATG GCT GCA AAA TTG GAA GCT GAG GTA CGT GCA AGA  3144
996   S   C   I   R   R   A   I   S   M   A   A   K   L   E   A   E   V   R   A   R    1015

3145  GAG AGA AAT ACA CGC ATG GGA GAA CCA GAA GGA CAT GAA GAA CCG AGA GGC GCA GAA GAA  3204
1016  E   R   N   T   R   M   G   E   P   E   G   H   E   E   P   R   G   A   E   E    1035

3205  TCT ATT TCG GCT CTA GGT GAC TTG TTT GCA GAC CTG AAA TTT GCT CTC TCT GAA GAG GAC  3264
1036  S   I   S   A   L   G   D   L   F   A   D   L   K   F   A   L   S   E   E   D    1055

3265  CCT TGG AAA GCA TTC GAG TTT TTA AAG CAT GCT TGG AAG ATT GCT GGC AAA ATC AGA CTA  3324
1056  P   W   K   A   F   E   F   L   K   H   A   W   K   I   A   G   K   I   R   L    1075

3325  AAA CCA ACT TGT TCA TTT TGA TTTAATCTTAACATTATAGCAACTGCAAGGTCTTGATCATCTGTTAGTTGCG  3397
1076  K   P   T   C   S   F   *                                                           1082

3398  TACTAACTT ATG TGT ATT AGT ATA ACA AGA AAA GAG AAT TAG AGAG ATG GAT TCT AAT CCG  3458
1             M   C   I   S   I   T   R   K   E   N   *        M   D   S   N   P    5

3459  GTG TTG CAG TAC ATC TTT TCT CCA CCC GCA TAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  3522
6     V   L   Q   Y   I   F   S   P   P   A   *                                        16
```

Figure 4 (Continued)

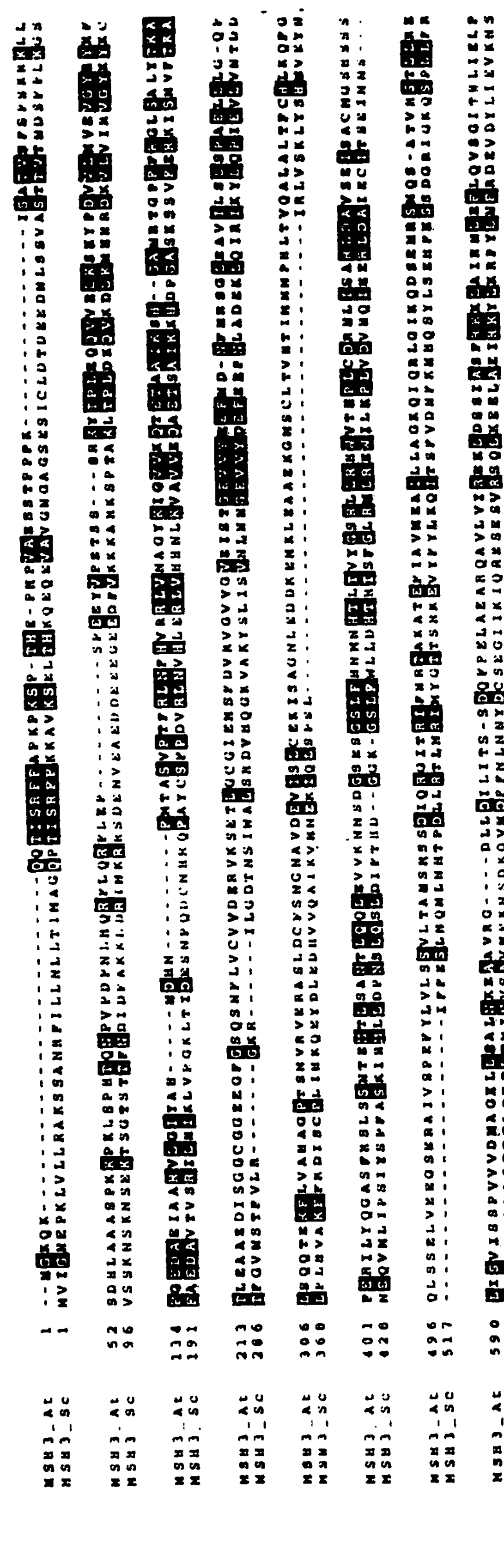
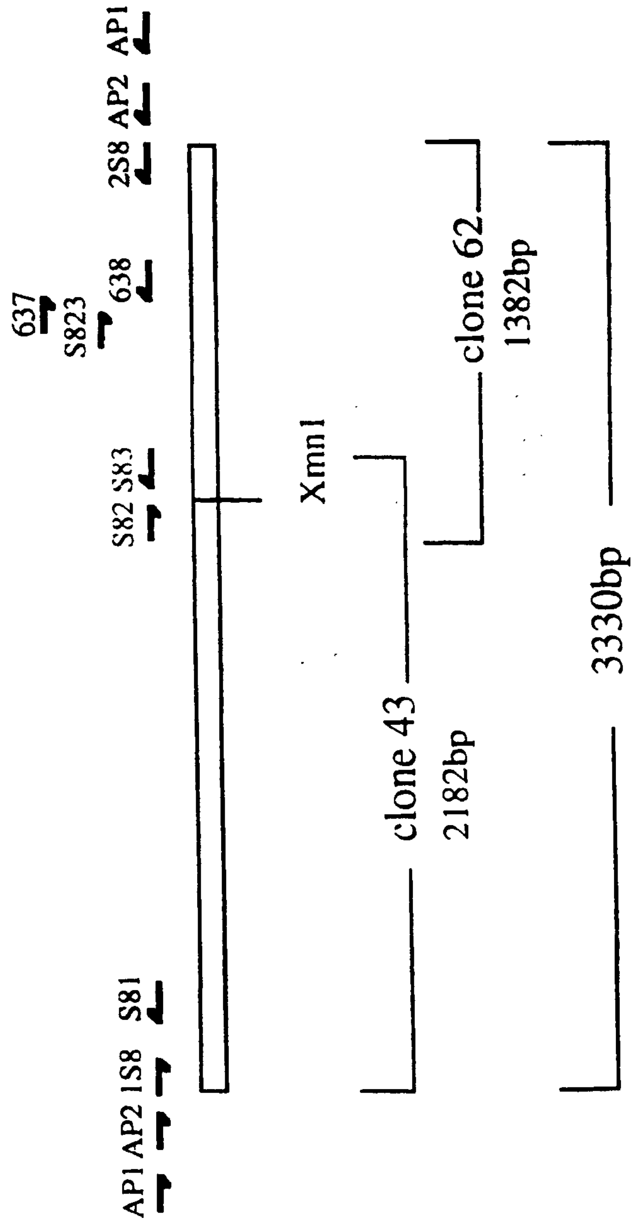


Figure 5

Figure 6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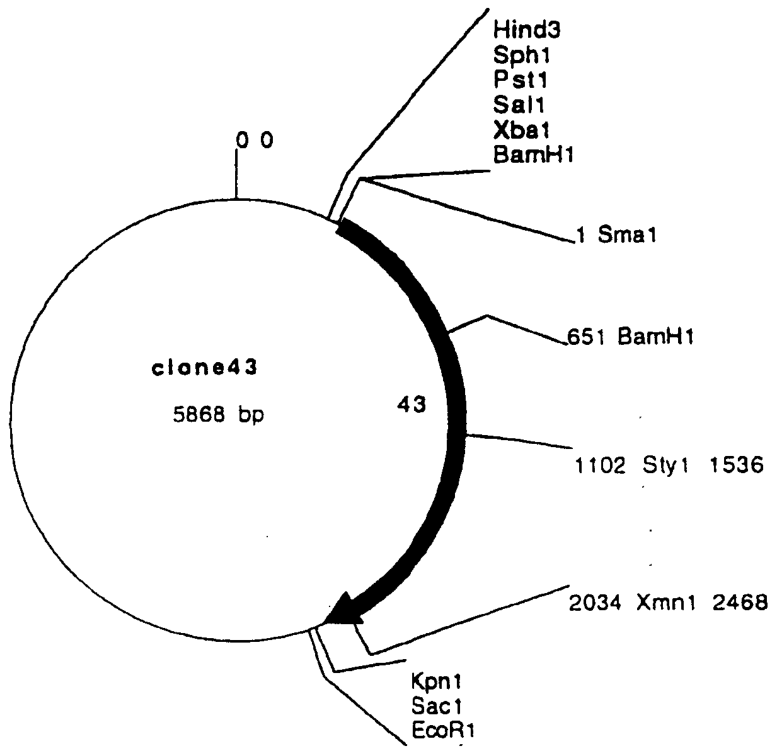

Figure 7

Comments/References: 43= 5' side of S8 (AtMSH6) 2182 bp in pUC18/Sma1

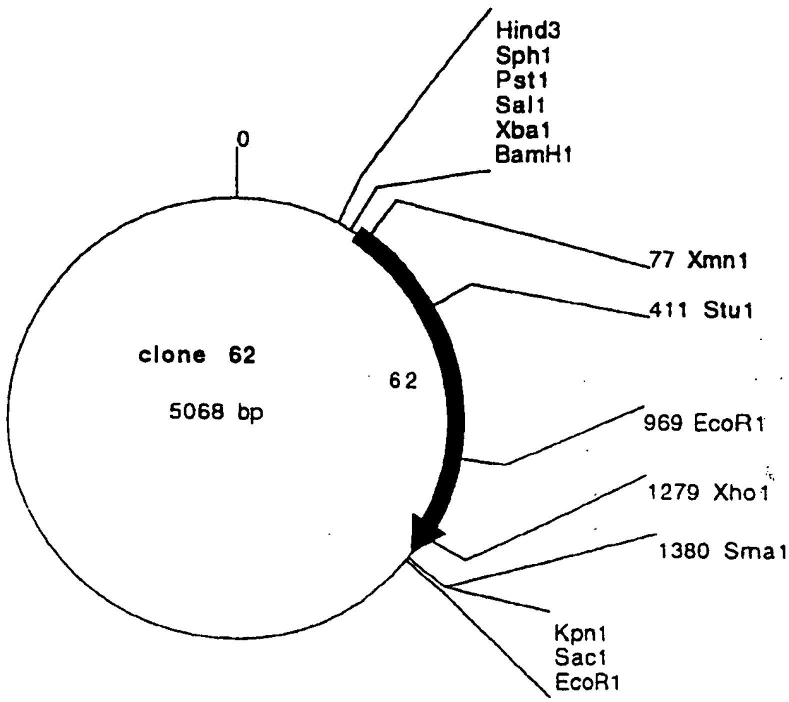

Figure 8

Comments/References: 62= 3' side of S8 (AtMSH6) 1379bp in pUC18/Sma1

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1    AAAAGTTGAGCCCTGAGGAGTATCGTTTCCGCCATTTCTACGACGCAAGGCGAAAATTTTTGGCGCCAATCTTTCCCCCC  80
81   TTTCGAATTCTCTCAGCTCAAAACATCGTTTCTCTCTCACTCTCTCTCACAATTCCAAAAA ATG CAG CGC CAG  153
1                                                                  M   Q   R   Q    4

154  AGA TCG ATT TTG TCT TTC TTC CAA AAA CCC ACC GCG GCG ACT ACG AAG GGT TTG GTT TCC  213
5    R   S   I   L   S   F   F   Q   K   P   T   A   A   T   T   K   G   L   V   S    24

214  GGC GAT GCT GCT AGC GGC GGG GGC GGC AGC GGA GGA CCA CGA TTT AAT GTG AAG GAA GGG  273
25   G   D   A   A   S   G   G   G   G   S   G   G   P   R   F   N   V   R   E   G    44

274  GAT GCT AAA GGC GAC GCT TCT GTA CGT TTT GCT GTT TCG AAA TCT GTC GAT GAG GTT AGA  333
45   D   A   K   G   D   A   S   V   R   F   A   V   S   K   S   V   D   E   V   R    64

334  GGA ACG GAT ACT CCA CCG GAG AAG GTT CCG CGT CGT GTC CTG CCG TCT GGA TTT AAG CCG  393
65   G   T   D   T   P   P   E   K   V   P   R   R   V   L   P   S   G   F   K   P    84

394  GCT GAA TCC GCC GST GAT GCT TCG TCC CTG TTC TCC AAT ATT ATG CAT AAG TTT GTA AAA  453
85   A   E   S   A   G   D   A   S   S   L   F   S   N   I   M   H   K   F   V   K    104

454  GTC GAT GAT CGA GAT TGT TCT GGA GAG AGG AGC CGA GAA GAT GTT GTT CCG CTG AAT GAT  513
105  V   D   D   R   D   C   S   G   E   R   S   R   E   D   V   V   P   L   N   D    124

514  TCA TCT CTA TGT ATG AAG GCT AAT GAT GTT ATT CCT CAA TTT CGT TCC AAT AAT GGT AAA  573
125  S   S   L   C   M   K   A   N   D   V   I   P   Q   F   R   S   N   N   G   K    144

574  ACT CAA GAA AGA AAC CAT GCT TTT AGT TTC AGT GGG AGA GCT GAA CTT AGA TCA GTA GAA  633
145  T   Q   E   R   N   H   A   F   S   F   S   G   R   A   E   L   R   S   V   E    164

634  GAT ATA GGA GTA GAT GGC GAT GTT CCT GGT CCA GAA ACA CCA GGG ATG CGT CCA CGT GCT  693
165  D   I   G   V   D   G   D   V   P   G   P   E   T   P   G   M   R   P   R   A    184

694  TCT CGC TTG AAG CGA GTT CTG GAG GAT GAA ATG ACT TTT AAG GAG GAT AAG GTT CCT GTA  753
185  S   R   L   K   R   V   L   E   D   E   M   T   F   K   E   D   K   V   P   V    204

754  TTG GAC TCT AAC AAA AGG CTG AAA ATG CTC CAG GAT CCG GTT TGT GGA GAG AAG AAA GAA  813
205  L   D   S   N   K   R   L   K   M   L   Q   D   P   V   C   G   E   K   K   E    224

814  GTA AAC GAA GGA ACC AAA TTT GAA TGG CTT GAG TCT TCT CGA ATC AGG GAT GCC AAT AGA  873
225  V   N   E   G   T   K   F   E   W   L   E   S   S   R   I   R   D   A   N   R    244

874  AGA CGT CCT GAT GAT CCC CTT TAC GAT AGA AAG ACC TTA CAC ATA CCA CCT GAT GTT TTC  933
245  R   R   P   D   D   P   L   Y   D   R   K   T   L   H   I   P   P   D   V   F    264
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Figure 9

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 934 AAG AAA ATG TCT GCA TCA CAA AAG CAA TAT TGG AGT GTT AAG AGT GAA TAT ATG GAC ATT  993
 265  K   K   M   S   A   S   Q   K   Q   Y   W   S   V   K   S   E   Y   M   D   I   284

 996 GTG CTT TTC TTT AAA GTG GGG AAA TTT TAT GAG CTG TAT GAG CTA GAT GCG GAA TTA GGT 1053
 285  V   L   F   F   K   V   G   K   F   Y   E   L   Y   E   L   D   A   E   L   G   304

1054 CAC AAG GAG CTT GAC TGG AAG ATG ACC ATG AGT GGT GTG GGA AAA TGC AGA CAG GTT GGT 1113
 305  H   K   E   L   D   W   K   M   T   M   S   G   V   G   K   C   R   Q   V   G   324

1114 ATC TCT GAA AGT GGG ATA GAT GAG GCA GTG CAA AAG CTA TTA GCT CGT GGA TAT AAA GTT 1173
 325  I   S   E   S   G   I   D   E   A   V   Q   K   L   L   A   R   G   Y   K   V   344

1174 GGA CGA ATC GAG CAG CTA GAA ACA TCT GAC CAA GCA AAA GCC AGA GGT GCT AAT ACT ATA 1233
 345  G   R   I   E   Q   L   E   T   S   D   Q   A   K   A   R   G   A   N   T   I   364

1234 ATT CCA AGG AAG CTA GTT CAG GTA TTA ACT CCA TCA ACA GCA AGC GAG GGA AAC ATC GGG 1293
 365  I   P   R   K   L   V   Q   V   L   T   P   S   T   A   S   E   G   N   I   G   384

1294 CCT GAT GCC GTC CAT CTT CTT GCT ATA AAA GAG ATC AAA ATG GAG CTA CAA AAG TGT TCA 1353
 385  P   D   A   V   H   L   L   A   I   K   E   I   K   M   E   L   Q   K   C   S   404

1354 ACT GTG TAT GGA TTT GCT TTT GTT GAC TGT GCT GCC TTG AGG TTT TGG GTT GGG TCC ATC 1413
 405  T   V   Y   G   F   A   F   V   D   C   A   A   L   R   F   W   V   G   S   I   424

1414 AGC GAT GAT GCA TCA TGT GCT GCT CTT GGA GCG TTA TTG ATG CAG GTT TCT CCA AAG GAA 1473
 425  S   D   D   A   S   C   A   A   L   G   A   L   L   M   Q   V   S   P   K   E   444

1474 GTG TTA TAT GAC AGT AAA GGG CTA TCA AGA GAA GCA CAA AAG GCT CTA AGG AAA TAT ACG 1533
 445  V   L   Y   D   S   K   G   L   S   R   E   A   Q   K   A   L   R   K   Y   T   464

1534 TTG ACA GGG TCT ACG GCG GTA CAG TTG GCT CCA GTA CCA CAA GTA ATG GGG GAT ACA GAT 1593
 465  L   T   G   S   T   A   V   Q   L   A   P   V   P   Q   V   M   G   D   T   D   484

1594 GCT GCT GGA GTT AGA AAT ATA ATA GAA TCT AAC GGA TAC TTT AAA GGT TCT TCT GAA TCA 1653
 485  A   A   G   V   R   N   I   I   E   S   N   G   Y   F   K   G   S   S   E   S   504

1654 TGG AAC TGT GCT GTT GAT GGT CTA AAT GAA TGT GAT GTT GCC CTT AGT GCT CTT GGA GAG 1713
 505  W   N   C   A   V   D   G   L   N   E   C   D   V   A   L   S   A   L   G   E   524

1714 CTA ATT AAT CAT CTG TCT AGG CTA AAG CTA GAA GAT GTA CTT AAG CAT GGG GAT ATT TTT 1773
 525  L   I   N   H   L   S   R   L   K   L   E   D   V   L   K   H   G   D   I   F   544

1774 CCA TAC CAA GTT TAC AGG GGT TGT CTC AGA ATT GAT GGC CAG ACG ATG GTA AAT CTT GAG 1833
 545  P   Y   Q   V   Y   R   G   C   L   R   I   D   G   Q   T   M   V   N   L   E   564
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Figure 9 (Continued)

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1834  ATA TTT AAC AAT AGC TGT GAT GGT GGT CCT TCA GGG ACC TTG TAC AAA TAT CTT GAT AAC  1893
 565  I   F   N   N   S   C   D   G   G   P   S   G   T   L   Y   K   Y   L   D   N     584

1894  TGT GTT AGT CCA ACT GGT AAG CGA CTC TTA AGG AAT TGG ATC TGC CAT CCA CTC AAA GAT  1953
 585  C   V   S   P   T   G   K   R   L   L   R   N   W   I   C   H   P   L   K   D     604

1954  GTA GAA AGC ATC AAT AAA CGG CTT GAT GTA GTT GAA GAA TTC ACG GCA AAC TCA GAA AGT  2013
 605  V   E   S   I   N   K   R   L   D   V   V   E   E   F   T   A   N   S   E   S     624

2014  ATG CAA ATC ACT GGC CAG TAT CTC CAC AAA CTT CCA GAC TTA GAA AGA CTG CTC GGA CGC  2073
 625  M   Q   I   T   G   Q   Y   L   H   K   L   P   D   L   E   R   L   L   G   R     644

2074  ATC AAG TCT AGC GTT CGA TCA TCA GCC TCT GTG TTG CCT GCT CTT CTG GGG AAA AAA GTG  2133
 645  I   K   S   S   V   R   S   S   A   S   V   L   P   A   L   L   G   K   K   V     664

2134  CTG AAA CAA CGA GTT AAA GCA TTT GGC CAA ATT GTG AAA GGG TTC AGA AGT GGA ATT GAT  2193
 665  L   K   Q   R   V   K   A   F   G   Q   I   V   K   G   F   R   S   G   I   D     684

2194  CTG TTG TTG GCT CTA CAG AAG GAA TCA AAT ATG ATG AGT TTG CTT TAT AAA CTC TGT AAA  2253
 685  L   L   L   A   L   Q   K   E   S   N   M   M   S   L   L   Y   K   L   C   K     704

2254  CTT CCT ATA TTA GTA GGA AAA AGC GGG CTA GAG TTA TTT CTT TCT CAA TTC GAA GCA GCC  2313
 705  L   P   I   L   V   G   K   S   G   L   E   L   F   L   S   Q   F   E   A   A     724

2314  ATA GAT AGC GAC TTT CCA AAT TAT CAG AAC CAA GAT GTG ACA GAT GAA AAC GCT GAA ACT  2373
 725  I   D   S   D   F   P   N   Y   Q   N   Q   D   V   T   D   E   N   A   E   T     744

2374  CTC ACA ATA CTT ATC GAA CTT TTT ATC GAA AGA GCA ACT CAA TGG TCT GAG GTC ATT CAC  2433
 745  L   T   I   L   I   E   L   F   I   E   R   A   T   Q   W   S   E   V   I   H     764

2434  ACC ATA AGC TGC CTA GAT GTC CTG AGA TCT TTT GCA ATC GCA GCA AGT CTC TCT GCT GGA  2493
 765  T   I   S   C   L   D   V   L   R   S   F   A   I   A   A   S   L   S   A   G     784

2494  AGC ATG GCC AGG CCT GTT ATT TTT CCC GAA TCA GAA GCT ACA GAT CAG AAT CAG AAA ACA  2553
 785  S   M   A   R   P   V   I   F   P   E   S   E   A   T   D   Q   N   Q   K   T     804

2554  AAA GGG CCA ATA CTT AAA ATC CAA GGA CTA TGG CAT CCA TTT GCA GTT GCA GCC GAT GGT  2613
 805  K   G   P   I   L   K   I   Q   G   L   W   H   P   F   A   V   A   A   D   G     824

2614  CAA TTG CCT GTT CCG AAT GAT ATA CTC CTT GGC GAG GCT AGA AGA AGC AGT GGC AGC ATT  2673
 825  Q   L   P   V   P   N   D   I   L   L   G   E   A   R   R   S   S   G   S   I     844

2674  CAT CCT CGG TCA TTG TTA CTG ACG GGA CCA AAC ATG GGC GGA AAA TCA ACT CTT CTT CGT  2733
 845  H   P   R   S   L   L   L   T   G   P   N   M   G   G   K   S   T   L   L   R     864
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Figure 9 (Continued)

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2734 GCA ACA TGT CTG GCC GTT ATC TTT GCC CAA CTT GGC TGC TAC GTG CCG TGT GAG TCT TGC 2793
 865 A   T   C   L   A   V   I   F   A   Q   L   G   C   Y   V   P   C   E   S   C    884

2794 GAA ATC TCC CTC GTG GAT ACT ATC TTC ACA AGG CTT GGC GCA TCT GAT AGA ATC ATG ACA 2853
 885 E   I   S   L   V   D   T   I   F   T   R   L   G   A   S   D   R   I   M   T    904

2854 GGA GAG AGT ACC TTT TTG GTA GAA TGC ACT GAG ACA GCG TCA GTT CTT CAG AAT GCA ACT 2913
 905 G   E   S   T   F   L   V   E   C   T   E   T   A   S   V   L   Q   N   A   T    924

2914 CAG GAT TCA CTA GTA ATC CTT GAC GAA CTG GGC AGA GGA ACT AGT ACT TTC GAT GGA TAC 2973
 925 Q   D   S   L   V   I   L   D   E   L   G   R   G   T   S   T   F   D   G   Y    944

2974 GCC ATT GCA TAC TCG GTT TTT CGT CAC CTG GTA GAG AAA GTT CAA TGT CGG ATG CTC TTT 3033
 945 A   I   A   Y   S   V   F   R   H   L   V   E   K   V   Q   C   R   M   L   F    964

3034 GCA ACA CAT TAC CAC CCT CTC ACC AAG GAA TTC GCG TCT CAC CCA CGT GTC ACC TCG AAA 3093
 965 A   T   H   Y   H   P   L   T   K   E   F   A   S   H   P   R   V   T   S   K    984

3094 CAC ATG GCT TGC GCA TTC AAA TCA AGA TCT GAT TAT CAA CCA CGT GGT TGT GAT CAA GAC 3153
 985 H   M   A   C   A   F   K   S   R   S   D   Y   Q   P   R   G   C   D   Q   D   1004

3154 CTA GTG TTC TTG TAC CGT TTA ACC GAG GGA GCT TGT CCT GAG AGC TAC GGA CTT CAA GTG 3213
1005 L   V   F   L   Y   R   L   T   E   G   A   C   P   E   S   Y   G   L   Q   V   1024

3214 GCA CTC ATG GCT GGA ATA CCA AAC CAA GTG GTT GAA ACA GCA TCA GGT GCT GCT CAA GCC 3273
1025 A   L   M   A   G   I   P   N   Q   V   V   E   T   A   S   G   A   A   Q   A   1044

3274 ATG AAG AGA TCA ATT GGG GGA AAC TTC AAG TCA AGT GAG CTA AGA TCT GAG TTC TCA AGT 3333
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3334 CTG CAT GAA GAC TGG CTC AAG TCA TTG GTG GGT ATT TCT CGA GTC GCC CAC AAC AAT GCC 3393
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3394 CCC ATT GGC GAA GAT GAC TAC GAC ACT TTG TTT TGC TTA TGG CAT GAG ATC AAA TCC TCT 3453
1085 P   I   G   E   D   D   Y   D   T   L   F   C   L   W   H   E   I   K   S   S   1104

3454 TAC TGT GTT CCC AAA TAA ATG GCT ATG ACA TAA CACTATCTGAAGCTCGTTAAGTCTTTTGCCTCTCT 3521
1105 Y   C   V   P   K   *   M   A   M   T   *                                          5

3522 G ATG TTT ATT CCT CTT AAA AAA TGC TTA TAT ATC AAA AAA TTG TTT CCT CGA TTA AAA 3579
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Figure 9 (Continued)

Figure 10

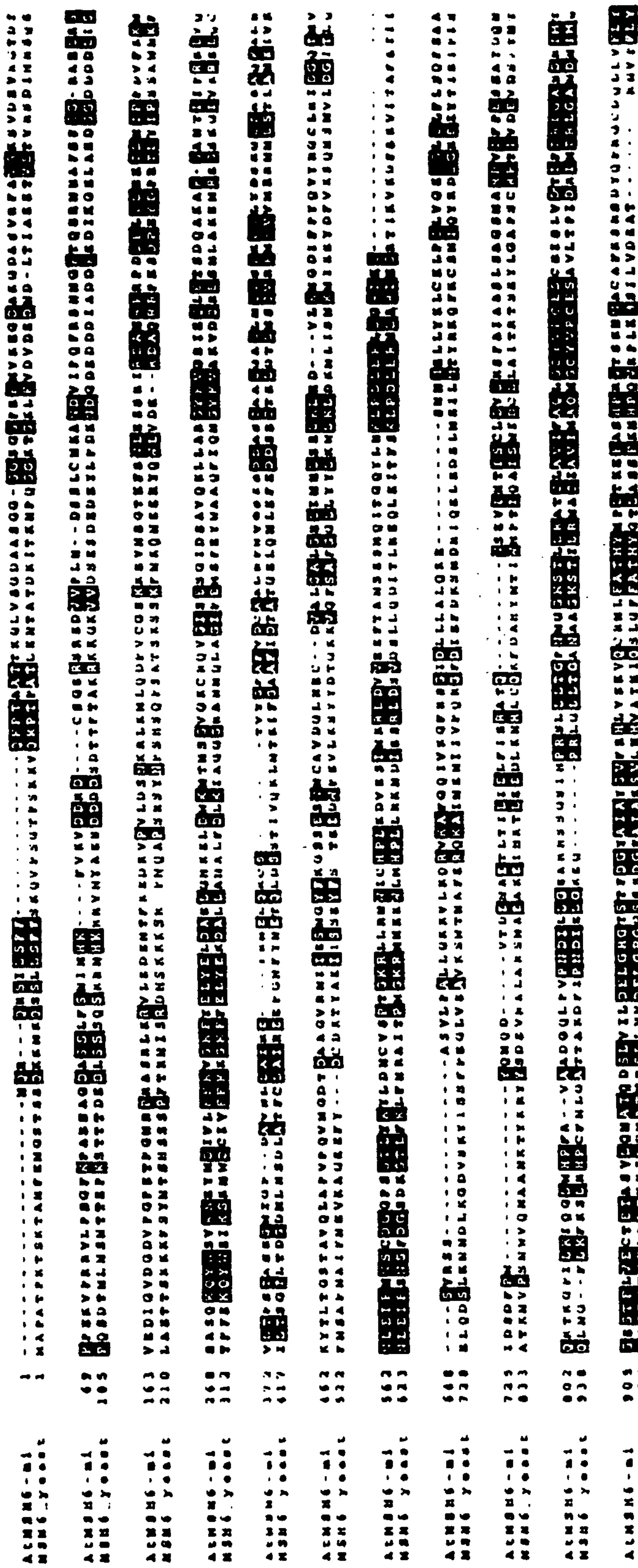

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Figure 11

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Figure 11 (Continued)

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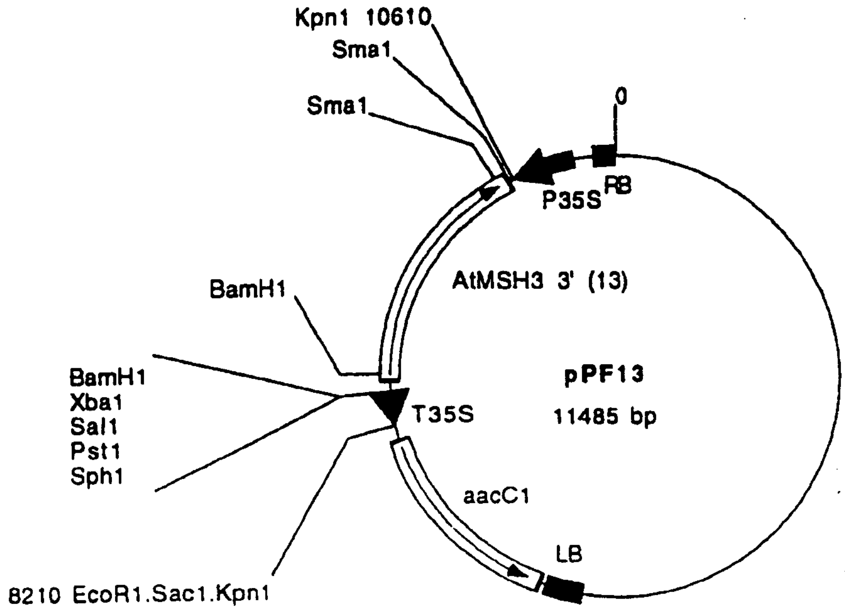


Figure 12

Comments/References: AtMSH3 3' side antisense : AtMSH3 3' (13 = 2104bp) from pUC18/13 Sal1/Sst1/T4 into pCW164 BamH1/T4 in Agrobacterium LBA4404

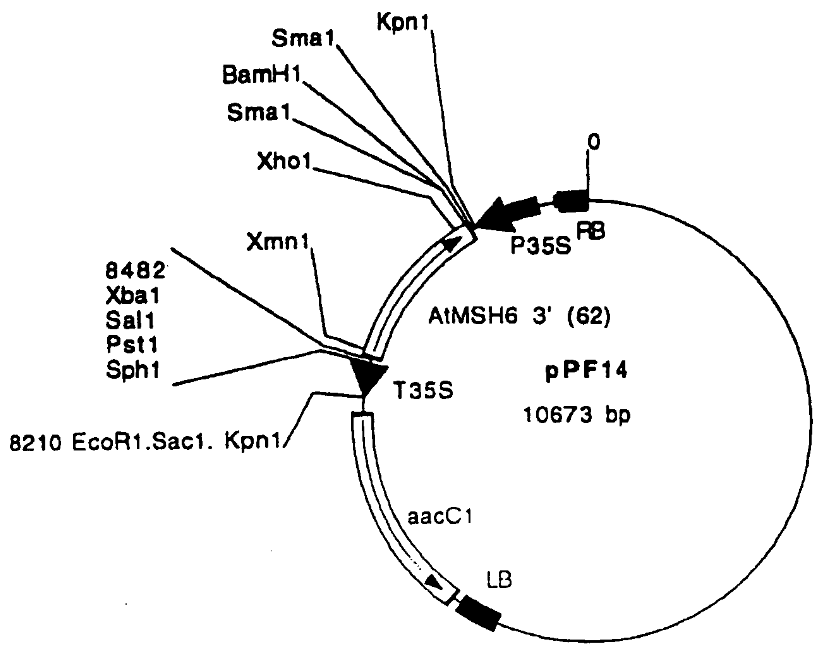


Figure 13

Comments/References: AtMSH6 (S8) 3' side antisens : 62 Sal1/Sst1/T4 (1379bp) into pCW164 BamH1/T4

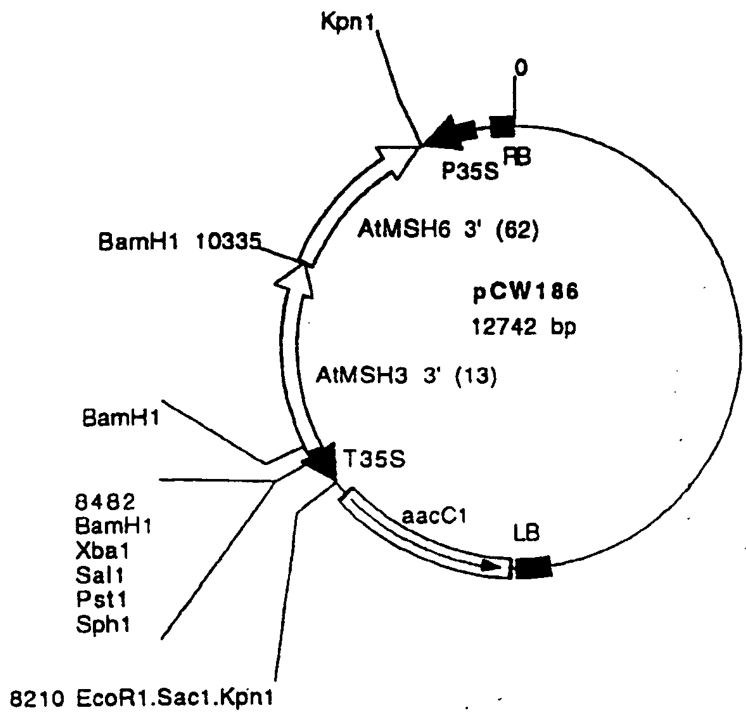


Figure 14

Comments/References: AtMSH6 3'/AtMSH3 3' antisense : AtMSH6 (S8) 3' side (62=1379bp) Sal1/Sst1/T4 into pPF13 (pCW164 AtMSH3 (S5) 3' side (13=2104) antisens)/Sma1. in LBA4404

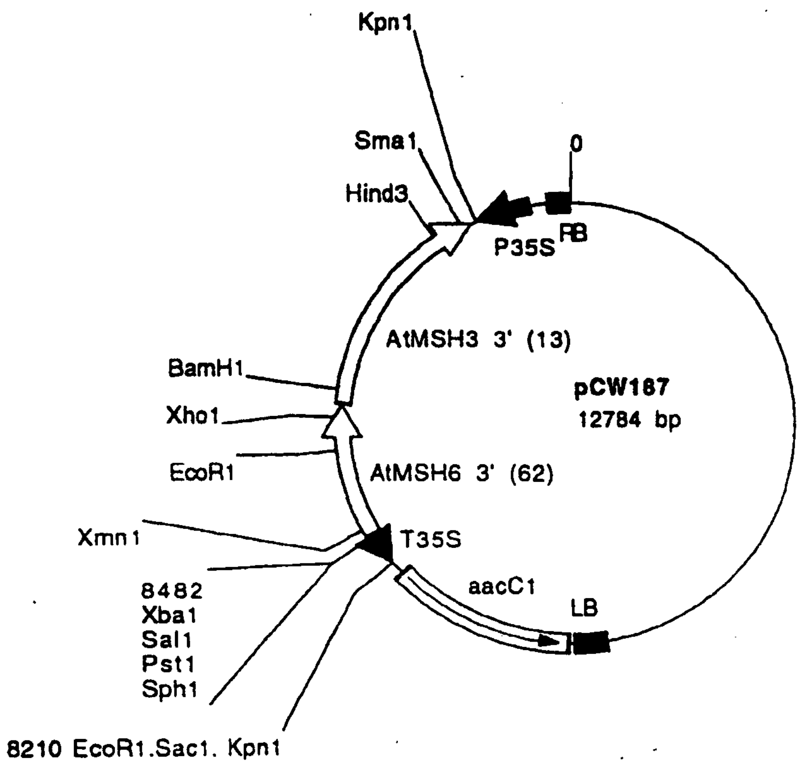


Figure 15

Comments/References: AtMSH3 3'/AtMSH6 3' antisens (D) : AtMSH3 (S5) 3' side (13=2104bp) Sal1/Sst1/T4 into pPF14 (AtMSH6 (S8) 3'side (62=1379bp) antisense into pCW164)/Sma1. in LBA4404

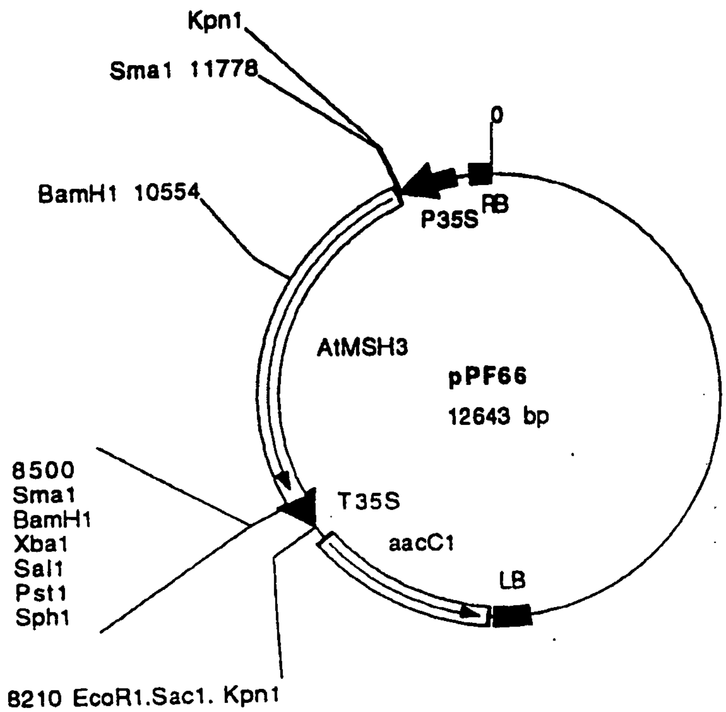


Figure 16

Comments/References: AtMSH3 (S8) complete, sense orientation : pPF26 (3342bp) Sma1 into pCW164 Sma1

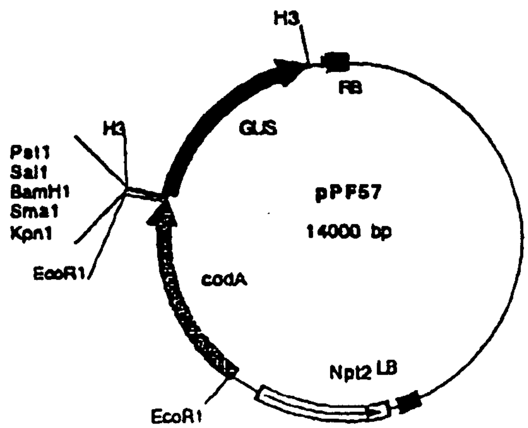
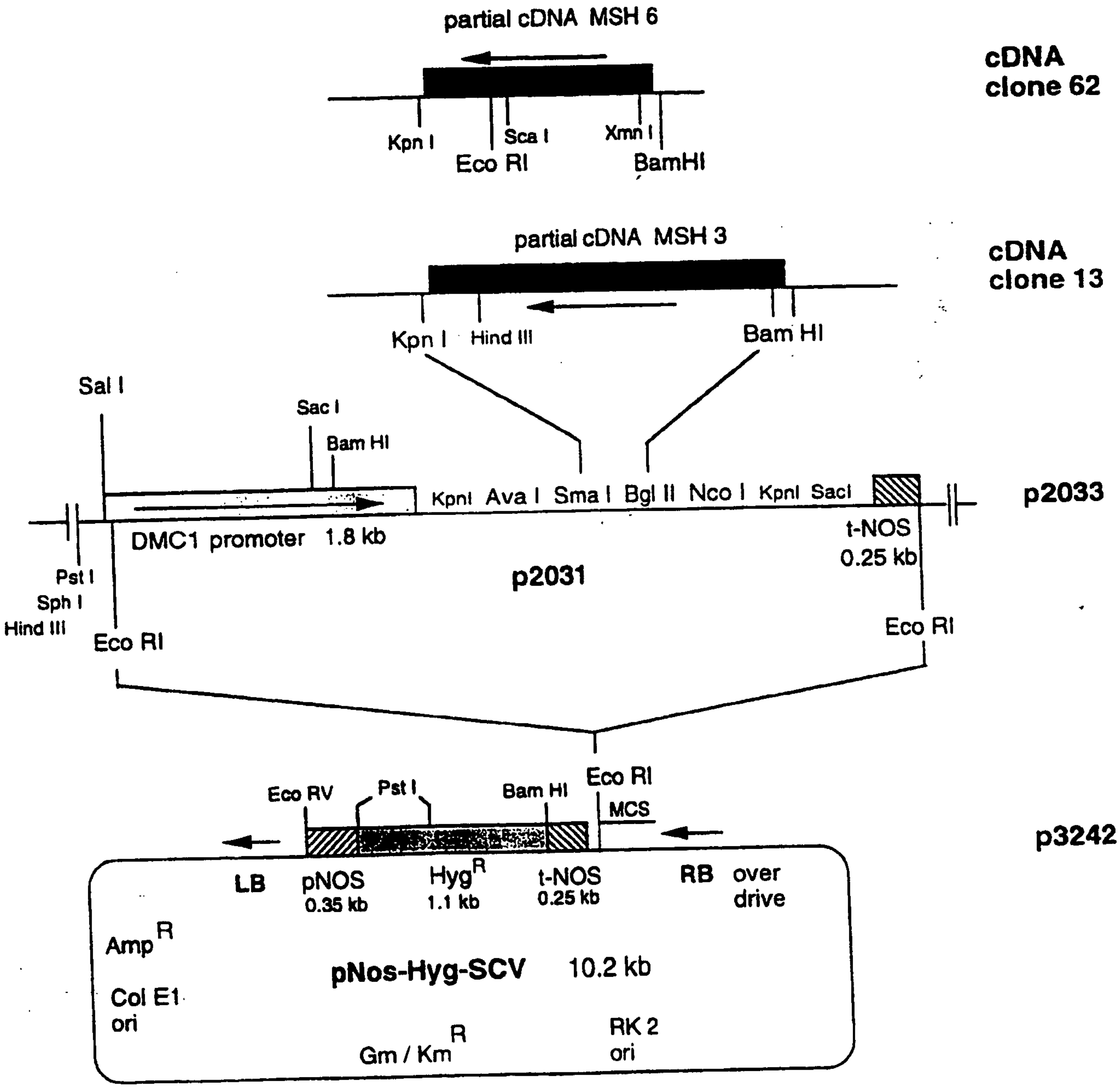


Figure 17

Comments/References: pPZP111 with codA EcoR1 cassette in EcoR1 site and Hind3 GUS cassette in Hind3 site. KanR. All genes under Promoter/terminator 35S

Figure 18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Xmn I
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t-NOS 0.25 kb
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Sph I
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Pst I
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Eco RI
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LB
pNOS 0.35 kb
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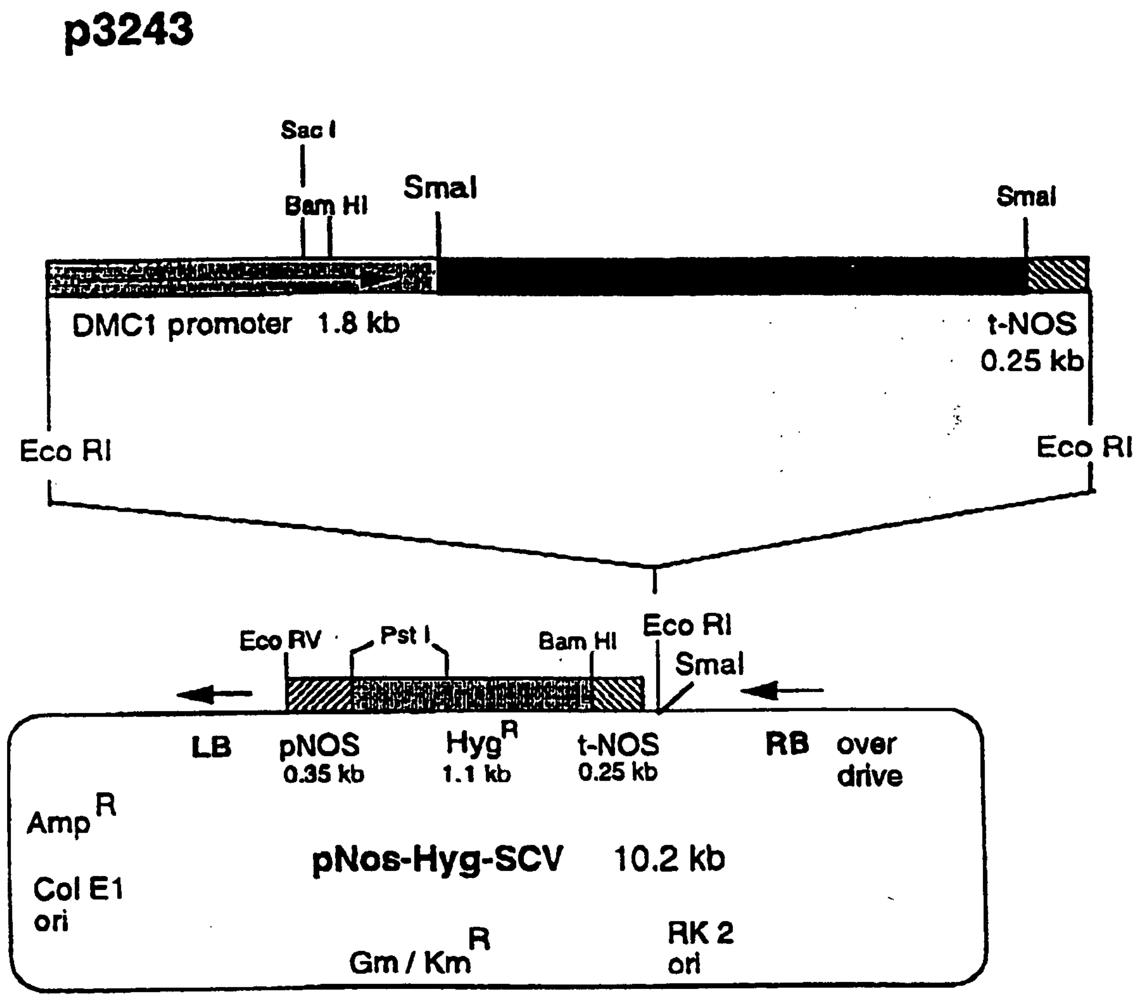
Gm / Km R
RK 2 ori

Figure 19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<223> MSH3 specific primer 1S5 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 10

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<210> 11
<211> 27
<212> DNA
<213> Artificial sequence

<220>
<223> MSH3 specific primer S53 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 11

gacaaagagc gaaatgaggc cccttgg 27

<210> 12
<211> 1250
<212> DNA
<213> Arabidopsis thaliana ecotype Columbia
<223> Clone 52

<400> 12

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gccactgtat ccttctctcc ttccaagcgt aagcttctct ccgaccacct cgccgccgcg 180

tcacccaaaa agcctaaact ttctcctcac actcaaaacc cagtacccga tcccaattta 240

caccaaagat ttctccagag atttctggaa ccctcgccgg aggaatatgt tcccgaaacg 300

tcatcatcga ggaaatacac accattggaa cagcaagtgg tggagctaaa gagcaagtac 360

ccagatgtgg ttttgatggt ggaagttggt tacaggtaca gattcttcgg agaagacgcg 420

gagatcgcag cacgcgtgtt gggtatttac gctcatatgg atcacaattt catgacggcg 480

agtgtgccaa catttcgatt gaatttccat gtgagaagac tggtgaatgc aggatacaag 540

attggtgtag tgaagcagac tgaaactgca gccattaagt cccatggtgc aaaccggacc 600

ggcccttttt tccggggact gtcggcgttg tataccaaag ccacgcttga agcggctgag 660

gatataagtg gtggttgtgg tggtgaagaa ggttttggtt cacagagtaa tttcttggtt 720

tgtgttgtgg atgagagagt taagtcggag acattaggct gtggtattga aatgagtttt 780

gatgttagag tcggtgttgt tggcgttgaa atttcgacag gtgaagttgt ttatgaagag 840

ttcaatgata atttcatgag aagtggatta gaggctgtga ttttgagctt gtcaccagct 900

gagctgttgc ttggccagcc tctttcacaa caaactgaga agtttttggt ggcacatgct 960

ggacctacct caaacgttcg agtggaacgt gcctcactgg attgtttcag caatggtaat 1020

gcagtagatg aggttatttc attatgtgaa aaaatcagcg caggtaactt agaagatgat 1080

aaagaaatga agctggaggc tgctgaaaaa ggaatgtctt gcttgacagt tcatacaatt 1140

atgaacatgc cacatctgac tgttcaagcc ctcgccctaa cgttttgcca tctcaaacag 1200

tttggatttg aaaggatcct ttaccaaggg gcctcatttc gctctttgtc 1250

<210> 13
<211> 34
<212> DNA
<213> Artificial sequence

<220>
<223> MSH3 specific primer 2S5 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 13

atcccgggtc aaaatgaaca agttggtttt agtc 34

<210> 14
<211> 27
<212> DNA
<213> Artificial sequence

<220>
<223> MSH3 specific primer S52 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 14

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<210> 15
<211> 2110
<212> DNA
<213> *Arabidopsis thaliana* ecotype Columbia
<223> Clone 13

<400> 15

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tgaaaggatc ctttaccaag gggcctcatt tcgctctttg tcaagtaaca cagagatgac 120

tctctcagcc aatactctgc aacagttgga ggttgtgaaa aataattcag atggatcgga 180

atctggctcc ttattccata atatgaatca cacacttaca gtatatggtt ccaggcttct 240

tagacactgg gtgactcatc ctctatgcga tagaaatttg atatctgctc ggcttgatgc 300

tgtttctgag atttctgctt gcatgggatc tcatagttct tcccagctca gcagtgagtt 360

ggttgaagaa ggttctgaga gagcaattgt atcacctgag ttttatctcg tgctctcctc 420

agtcttgaca gctatgtcta gatcatctga tattcaacgt ggaataacaa gaatctttca 480

tcggactgct aaagccacag agttcattgc agttatggaa gctattttac ttgcggggaa 540

gcaaattcag cggcttggca taaagcaaga ctctgaaatg aggagtatgc aatctgcaac 600

tgtgcgatct actcttttga gaaaattgat ttctgttatt tcatcccctg ttgtggttga 660

caatgccgga aaacttctct ctgccctaaa taaggaagcg gctgttcgag gtgacttgct 720

cgacatacta atcacttcca gcgaccaatt tcctgagctt gctgaagctc gccaagcagt 780

tttagtcatc agggaaaagc tggattcctc gatagcttca tttcgcaaga agctcgctat 840

tcgaaatttg gaatttcttc aagtgtcggg gatcacacat ttgatagagc tgcccgttga 900

ttccaaggtc cctatgaatt gggtgaaagt aaatagcacc aagaagacta ttcgatatca 960

tcccccagaa atagtagctg gcttggatga gctagctcta gcaactgaac atcttgccat 1020

tgtgaaccga gcttcgtggg atagtttcct caagagtttc agtagatact acacagattt 1080

taaggctgcc gttcaagctc ttgctgcact ggactgtttg cactcccttt caactctatc 1140

tagaaacaag aactatgtcc gtcccgagtt tgtggatgac tgtgaaccag ttgagataaa 1200

catacagtct ggtcgtcatc ctgtactgga gactatatta caagataact tcgtcccaaa 1260

tgacacaatt ttgcatgcag aaggggaata ttgccaaatt atcaccggac ctaacatggg 1320

aggaaagagc tgctatatcc gtcaagttgc tttaatttcc ataatggctc aggttggttc 1380

ctttgtacca gcgtcattcg ccaagctgca cgtgcttgat ggtgttttca ctcggatggg 1440

tgcttcagac agtatccagc atggcagaag taccttttcta gaagaattaa gtgaagcgtc 1500

acacataatc agaacctgtt cttctcgttc gcttgttata ttagatgagc ttggaagagg 1560

cactagcaca cacgacggtg tagccattgc ctatgcaaca ttacagcatc tcctagcaga 1620

aaagagatgt ttggttcttt ttgtcacgca ttaccctgaa atagctgaga tcagtaacgg 1680

attcccaggt tctgttggga cataccatgt ctcgtatctg acattgcaga aggataaagg 1740

cagttatgat catgatgatg tgacctacct atataagctt gtgcgtggtc tttgcagcag 1800

gagctttggt tttaaggttg ctcagcttgc ccagatacct ccatcatgta tacgtcgagc 1860

catttcaatg gctgcaaaat tggaagctga ggtacgtgca agagagagaa atacacgcat 1920

gggagaacca gaaggacatg aagaaccgag aggcgcagaa gaatctattt cggctctagg 1980

tgacttgttt gcagacctga aatttgctct ctctgaagag gacccttgga aagcattcga 2040

gtttttaaag catgcttgga agattgctgg caaaatcaga ctaaaaccaa cttgttcatt 2100

ttgacccggg 2110

<210> 16
<211> 29
<212> DNA
<213> Artificial sequence

<220>
<223> MSH3 specific primer S51 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 16

ggatcgggta ctgggttttg agtgtgagg 29

<210> 17
<211> 30
<212> DNA
<213> Artificial sequence

<220>
<223> MSH3 specific primer S525 for PCR using cDNA of Arabidopsis thaliana ecotype Columbia

<400> 17

aggttctgat tatgtgtgac gctttactta 30

<210> 18
<211> 3522
<212> DNA
<213> *Arabidopsis thaliana* ecotype Columbia

<220>
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<222> (100)....(3342)
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catttctctt aaacggagga gattacgaat aaagcaatt 99

atg ggc aag caa aag cag cag acg att tct cgt ttc ttc gct ccc aaa 147
Met Gly Lys Gln Lys Gln Gln Thr Ile Ser Arg Phe Phe Ala Pro Lys
1 5 10 15

ccc aaa tcc ccg act cac gaa ccg aat ccg gta gcc gaa tca tca aca 195
Pro Lys Ser Pro Thr His Glu Pro Asn Pro Val Ala Glu Ser Ser Thr
20 25 30

ccg cca ccg aag ata tcc gcc act gta tcc ttc tct cct tcc aag cgt 243
Pro Pro Pro Lys Ile Ser Ala Thr Val Ser Phe Ser Pro Ser Lys Arg
35 40 45

aag ctt ctc tcc gac cac ctc gcc gcc gcg tca ccc aaa aag cct aaa 291
Lys Leu Leu Ser Asp His Leu Ala Ala Ala Ser Pro Lys Lys Pro Lys
50 55 60

ctt tct cct cac act caa aac cca gta ccc gat ccc aat tta cac caa 339
Leu Ser Pro His Thr Gln Asn Pro Val Pro Asp Pro Asn Leu His Gln
65 70 75 80

aga ttt ctc cag aga ttt ctg gaa ccc tcg ccg gag gaa tat gtt ccc 387
Arg Phe Leu Gln Arg Phe Leu Glu Pro Ser Pro Glu Glu Tyr Val Pro
85 90 95

gaa acg tca tca tcg agg aaa tac aca cca ttg gaa cag caa gtg gtg 435
Glu Thr Ser Ser Ser Arg Lys Tyr Thr Pro Leu Glu Gln Gln Val Val
100 105 110

gag cta aag agc aag tac cca gat gtg gtt ttg atg gtg gaa gtt ggt 483
Glu Leu Lys Ser Lys Tyr Pro Asp Val Val Leu Met Val Glu Val Gly
115 120 125

tac agg tac aga ttc ttc gga gaa gac gcg gag atc gca gca cgc gtg 531
Tyr Arg Tyr Arg Phe Phe Gly Glu Asp Ala Glu Ile Ala Ala Arg Val
130 135 140

ttg ggt att tac gct cat atg gat cac aat ttc atg acg gcg agt gtg 579
Leu Gly Ile Tyr Ala His Met Asp His Asn Phe Met Thr Ala Ser Val
145 150 155 160

cca aca ttt cga ttg aat ttc cat gtg aga aga ctg gtg aat gca gga 627
Pro Thr Phe Arg Leu Asn Phe His Val Arg Arg Leu Val Asn Ala Gly
165 170 175

tac aag att ggt gta gtg aag cag act gaa act gca gcc att aag tcc 675
Tyr Lys Ile Gly Val Val Lys Gln Thr Glu Thr Ala Ala Ile Lys Ser
180 185 190

cat ggt gca aac cgg acc ggc cct ttt ttc cgg gga ctg tcg gcg ttg 723
His Gly Ala Asn Arg Thr Gly Pro Phe Phe Arg Gly Leu Ser Ala Leu
195 200 205

tat acc aaa gcc acg ctt gaa gcg gct gag gat ata agt ggt ggt tgt 771
Tyr Thr Lys Ala Thr Leu Glu Ala Ala Glu Asp Ile Ser Gly Gly Cys
210 215 220

ggt ggt gaa gaa ggt ttt ggt tca cag agt aat ttc ttg gtt tgt gtt 819
Gly Gly Glu Glu Gly Phe Gly Ser Gln Ser Asn Phe Leu Val Cys Val
225 230 235 240

gtg gat gag aga gtt aag tcg gag aca tta ggc tgt ggt att gaa atg 867
Val Asp Glu Arg Val Lys Ser Glu Thr Leu Gly Cys Gly Ile Glu Met
245 250 255

agt ttt gat gtt aga gtc ggt gtt gtt ggc gtt gaa att tcg aca ggt 915
Ser Phe Asp Val Arg Val Gly Val Val Gly Val Glu Ile Ser Thr Gly
260 265 270

gaa gtt gtt tat gaa gag ttc aat gat aat ttc atg aga agt gga tta 963
Glu Val Val Tyr Glu Glu Phe Asn Asp Asn Phe Met Arg Ser Gly Leu
275 280 285

gag gct gtg att ttg agc ttg tca cca gct gag ctg ttg ctt ggc cag 1011
Glu Ala Val Ile Leu Ser Leu Ser Pro Ala Glu Leu Leu Leu Gly Gln
290 295 300

cct ctt tca caa caa act gag aag ttt ttg gtg gca atg gct gga cct 1059
Pro Leu Ser Gln Gln Thr Glu Lys Phe Leu Val Ala Met Ala Gly Pro
305 310 315 320

acc tca aac gtt cga gtg gaa cgt gcc tca ctg gat tgt ttc agc aat 1107
Thr Ser Asn Val Arg Val Glu Arg Ala Ser Leu Asp Cys Phe Ser Asn
325 330 335

ggt aat gca gta gat gag gtt att tca tta tgt gaa aaa atc agc gca 1155
Gly Asn Ala Val Asp Glu Val Ile Ser Leu Cys Glu Lys Ile Ser Ala
340 345 350

ggt aac tta gaa gat gat aaa gaa atg aag ctg gag gct gct gaa aaa 1203
Gly Asn Leu Glu Asp Asp Lys Glu Met Lys Leu Glu Ala Ala Glu Lys
355 360 365

gga atg tct tgc ttg aca gtt cat aca att atg aac atg cca cat ctg 1251
Gly Met Ser Cys Leu Thr Val His Thr Ile Met Asn Met Pro His Leu
370 375 380

act gtt caa gcc ctc gcc cta acg ttt tgc cat ctc aaa cag ttt gga 1299
Thr Val Gln Ala Leu Ala Leu Thr Phe Cys His Leu Lys Gln Phe Gly
385 390 395 400

ttt gaa agg atc ctt tac caa ggg gcc tca ttt cgc tct ttg tca agt 1347
Phe Glu Arg Ile Leu Tyr Gln Gly Ala Ser Phe Arg Ser Leu Ser Ser
405 410 415

aac aca gag atg act ctc tca gcc aat act ctg caa cag ttg gag gtt 1395
Asn Thr Glu Met Thr Leu Ser Ala Asn Thr Leu Gln Gln Leu Glu Val
420 425 430

gtg aaa aat aat tca gat gga tcg gaa tct ggc tcc tta ttc cat aat 1443
Val Lys Asn Asn Ser Asp Gly Ser Glu Ser Gly Ser Leu Phe His Asn
435 440 445

atg aat cac aca ctt aca gta tat gct tcc agg ctt ctt aga cac tgg 1491
Met Asn His Thr Leu Thr Val Tyr Gly Ser Arg Leu Leu Arg His Trp
450 455 460

gtg act cat cct cta tgc gat aga aat ttg ata tct gct cgg ctt gat 1539
Val Thr His Pro Leu Cys Asp Arg Asn Leu Ile Ser Ala Arg Leu Asp
465 470 475 480

gct gtt tct gag att tct gct tgc atg gga tct cat agt tct tcc cag 1587
Ala Val Ser Glu Ile Ser Ala Cys Met Gly Ser His Ser Ser Ser Gln
485 490 495

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ctc agc agt gag ttg gtt gaa gaa ggt tct gag aga gca att gta tca      1635
Leu Ser Ser Glu Leu Val Glu Glu Gly Ser Glu Arg Ala Ile Val Ser
            500                 505                 510

cct gag ttt tat ctc gtg ctc tcc tca gtc ttg aca gct atg tct aga      1683
Pro Glu Phe Tyr Leu Val Leu Ser Ser Val Leu Thr Ala Met Ser Arg
        515                 520                 525

tca tct gat att caa cgt gga ata aca aga atc ttt cat cgg act gct      1731
Ser Ser Asp Ile Gln Arg Gly Ile Thr Arg Ile Phe His Arg Thr Ala
    530                 535                 540

aaa gcc aca gag ttc att gca gtt atg gaa gct att tta ctt gcg ggg      1779
Lys Ala Thr Glu Phe Ile Ala Val Met Glu Ala Ile Leu Leu Ala Gly
545                 550                 555                 560

aag caa att cag cgg ctt ggc ata aag caa gac tct gaa atg agg agt      1827
Lys Gln Ile Gln Arg Leu Gly Ile Lys Gln Asp Ser Glu Met Arg Ser
                565                 570                 575

atg caa tct gca act gtg cga tct act ctt ttg aga aaa ttg att tct      1875
Met Gln Ser Ala Thr Val Arg Ser Thr Leu Leu Arg Lys Leu Ile Ser
            580                 585                 590

gtt att tca tcc cct gtt gtg gtt gac aat gcc gga aaa ctt ctc tct      1923
Val Ile Ser Ser Pro Val Val Val Asp Asn Ala Gly Lys Leu Leu Ser
        595                 600                 605

gcc cta aat aag gaa gcg gct gtt cga ggt gac ttg ctc gac ata cta      1971
Ala Leu Asn Lys Glu Ala Ala Val Arg Gly Asp Leu Leu Asp Ile Leu
    610                 615                 620

atc act tcc agc gac caa ttt cct gag ctt gct gaa gct cgc caa gca      2019
Ile Thr Ser Ser Asp Gln Phe Pro Glu Leu Ala Glu Ala Arg Gln Ala
625                 630                 635                 640

gtt tta gtc atc agg gaa aag ctg gat tcc tcg ata gct tca ttt cgc      2067
Val Leu Val Ile Arg Glu Lys Leu Asp Ser Ser Ile Ala Ser Phe Arg
                645                 650                 655

aag aag ctc gct att cga aat ttg gaa ttt ctt caa gtg tcg ggg atc      2115
Lys Lys Leu Ala Ile Arg Asn Leu Glu Phe Leu Gln Val Ser Gly Ile
            660                 665                 670

aca cat ttg ata gag ctg ccc gtt gat tcc aag gtc cct atg aat tgg      2163
Thr His Leu Ile Glu Leu Pro Val Asp Ser Lys Val Pro His Asn Trp
        675                 680                 685

gtg aaa gta aat agc acc aag aag act att cga tat cat ccc cca gaa      2211
Val Lys Val Asn Ser Thr Lys Lys Thr Ile Arg Tyr His Pro Pro Glu
    690                 695                 700
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ata gta gct ggc ttg gat gag cta gct cta gca act gaa cat ctt gcc 2259
Ile Val Ala Gly Leu Asp Glu Leu Ala Leu Ala Thr Glu His Leu Ala
705 710 715 720

att gtg aac cga gct tcg tgg gat agt ttc ctc aag agt ttc agt aga 2307
Ile Val Asn Arg Ala Ser Trp Asp Ser Phe Leu Lys Ser Phe Ser Arg
725 730 735

tac tac aca gat ttt aag gct gcc gtt caa gct ctt gct gca ctg gac 2355
Tyr Tyr Thr Asp Phe Lys Ala Ala Val Gln Ala Leu Ala Ala Leu Asp
740 745 750

tgt ttg cac tcc ctt tca act cta tct aga aac aag aac tat gtc cgt 2403
Cys Leu His Ser Leu Ser Thr Leu Ser Arg Asn Lys Asn Tyr Val Arg
755 760 765

ccc gag ttt gtg gat gac tgt gaa cca gtt gag ata aac ata cag tct 2451
Pro Glu Phe Val Asp Asp Cys Glu Pro Val Glu Ile Asn Ile Gln Ser
770 775 780

ggt cgt cat cct gta ctg gag act ata tta caa gat aac ttc gtc cca 2499
Gly Arg His Pro Val Leu Glu Thr Ile Leu Gln Asp Asn Phe Val Pro
785 790 795 800

aat gac aca att ttg cat gca gaa ggg gaa tat tgc caa att atc acc 2547
Asn Asp Thr Ile Leu His Ala Glu Gly Glu Tyr Cys Gln Ile Ile Thr
805 810 815

gga cct aac atg gga gga aag agc tgc tat atc cgt caa gtt gct tta 2595
Gly Pro Asn Met Gly Gly Lys Ser Cys Tyr Ile Arg Gln Val Ala Leu
820 825 830

att tcc ata atg gct cag gtt ggt tcc ttt gta cca gcg tca ttc gcc 2643
Ile Ser Ile Met Ala Gln Val Gly Ser Phe Val Pro Ala Ser Phe Ala
835 840 845

aag ctg cac gtg ctt gat ggt gtt ttc act cgg atg ggt gct tca gac 2691
Lys Leu His Val Leu Asp Gly Val Phe Thr Arg Met Gly Ala Ser Asp
850 855 860

agt atc cag cat ggc aga agt acc ttt cta gaa gaa tta agt gaa gcg 2739
Ser Ile Gln His Gly Arg Ser Thr Phe Leu Glu Glu Leu Ser Glu Ala
865 870 875 880

tca cac ata atc aga acc tgt tct tct cgt tcg ctt gtt ata tta gat 2787
Ser His Ile Ile Arg Thr Cys Ser Ser Arg Ser Leu Val Ile Leu Asp
885 890 895

gag ctt gga aga ggc act agc aca cac gac ggt gta gcc att gcc tat 2835
Glu Leu Gly Arg Gly Thr Ser Thr His Asp Gly Val Ala Ile Ala Tyr
900 905 910

gca aca tta cag cat ctc cta gca gaa aag aga tgt ttg gtt ctt ttt 2883
Ala Thr Leu Gln His Leu Leu Ala Glu Lys Arg Cys Leu Val Leu Phe
915 920 925

gtc acg cat tac cct gaa ata gct gag atc agt aac gga ttc cca ggt 2931
Val Thr His Tyr Pro Glu Ile Ala Glu Ile Ser Asn Gly Phe Pro Gly
930 935 940

tct gtt ggg aca tac cat gtc tcg tat ctg aca ttg cag aag gat aaa 2979
Ser Val Gly Thr Tyr His Val Ser Tyr Leu Thr Leu Gln Lys Asp Lys
945 950 955 960

ggc agt tat gat cat gat gat gtg acc tac cta tat aag ctt gtg cgt 3027
Gly Ser Tyr Asp His Asp Asp Val Thr Tyr Leu Tyr Lys Leu Val Arg
965 970 975

ggt ctt tgc agc agg agc ttt ggt ttt aag gtt gct cag ctt gcc cag 3075
Gly Leu Cys Ser Arg Ser Phe Gly Phe Lys Val Ala Gln Leu Ala Gln
980 985 990

ata cct cca tca tgt ata cgt cga gcc att tca atg gct gca aaa ttg 3123
Ile Pro Pro Ser Cys Ile Arg Arg Ala Ile Ser Met Ala Ala Lys Leu
995 1000 1005

gaa gct gag gta cgt gca aga gag aga aat aca cgc atg gga gaa cca 3171
Glu Ala Glu Val Arg Ala Arg Glu Arg Asn Thr Arg Met Gly Glu Pro
1010 1015 1020

gaa gga cat gaa gaa ccg aga ggc gca gaa gaa tct att tcg gct cta 3219
Glu Gly His Glu Glu Pro Arg Gly Ala Glu Glu Ser Ile Ser Ala Leu
1025 1030 1035 1040

ggt gac ttg ttt gca gac ctg aaa ttt gct ctc tct gaa gag gac cct 3267
Gly Asp Leu Phe Ala Asp Leu Lys Phe Ala Leu Ser Glu Glu Asp Pro
1045 1050 1055

tgg aaa gca ttc gag ttt tta aag cat gct tgg aag att gct ggc aaa 3315
Trp Lys Ala Phe Glu Phe Leu Lys His Ala Trp Lys Ile Ala Gly Lys
1060 1065 1070

atc aga cta aaa cca act tgt tca ttt tgatttaatc ttaacattat 3362
Ile Arg Leu Lys Pro Thr Cys Ser Phe
1075 1080

agcaactgca aggtcttgat catctgttag ttgcgtacta acttatgtgt attagtataa 3422

caagaaaaga gaattagaga gatggattct aatccggtgt tgcagtacat cttttctcca 3482

cccgcataaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3522

<210> 19
<211> 1081
<212> PRT

<213> *Arabidopsis thaliana* ecotype Columbia
<223> Polypeptide MSH3

<400> 19

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Pro Lys Ser Pro Thr His Glu Pro Asn Pro Val Ala Glu Ser Ser Thr
20 25 30

Pro Pro Pro Lys Ile Ser Ala Thr Val Ser Phe Ser Pro Ser Lys Arg
35 40 45

Lys Leu Leu Ser Asp His Leu Ala Ala Ala Ser Pro Lys Lys Pro Lys
50 55 60

Leu Ser Pro His Thr Gln Asn Pro Val Pro Asp Pro Asn Leu His Gln
65 70 75 80

Arg Phe Leu Gln Arg Phe Leu Glu Pro Ser Pro Glu Glu Tyr Val Pro
85 90 95

Glu Thr Ser Ser Ser Arg Lys Tyr Thr Pro Leu Glu Gln Gln Val Val
100 105 110

Glu Leu Lys Ser Lys Tyr Pro Asp Val Val Leu Met Val Glu Val Gly
115 120 125

Tyr Arg Tyr Arg Phe Phe Gly Glu Asp Ala Glu Ile Ala Ala Arg Val
130 135 140

Leu Gly Ile Tyr Ala His Met Asp His Asn Phe Met Thr Ala Ser Val
145 150 155 160

Pro Thr Phe Arg Leu Asn Phe His Val Arg Arg Leu Val Asn Ala Gly
165 170 175

Tyr Lys Ile Gly Val Val Lys Gln Thr Glu Thr Ala Ala Ile Lys Ser
180 185 190

His Gly Ala Asn Arg Thr Gly Pro Phe Phe Arg Gly Leu Ser Ala Leu
195 200 205

Tyr Thr Lys Ala Thr Leu Glu Ala Ala Glu Asp Ile Ser Gly Gly Cys
210 215 220

Gly Gly Glu Glu Gly Phe Gly Ser Gln Ser Asn Phe Leu Val Cys Val
225 230 235 240

Val Asp Glu Arg Val Lys Ser Glu Thr Leu Gly Cys Gly Ile Glu Met
245 250 255

Ser Phe Asp Val Arg Val Gly Val Val Gly Val Glu Ile Ser Thr Gly
260 265 270

Glu Val Val Tyr Glu Glu Phe Asn Asp Asn Phe Met Arg Ser Gly Leu
275 280 285

Glu Ala Val Ile Leu Ser Leu Ser Pro Ala Glu Leu Leu Leu Gly Gln
290 295 300

Pro Leu Ser Gln Gln Thr Glu Lys Phe Leu Val Ala Met Ala Gly Pro
305 310 315 320

Thr Ser Asn Val Arg Val Glu Arg Ala Ser Leu Asp Cys Phe Ser Asn
325 330 335

Gly Asn Ala Val Asp Glu Val Ile Ser Leu Cys Glu Lys Ile Ser Ala
340 345 350

Gly Asn Leu Glu Asp Asp Lys Glu Met Lys Leu Glu Ala Ala Glu Lys
355 360 365

Gly Met Ser Cys Leu Thr Val His Thr Ile Met Asn Met Pro His Leu
370 375 380

Thr Val Gln Ala Leu Ala Leu Thr Phe Cys His Leu Lys Gln Phe Gly
385 390 395 400

Phe Glu Arg Ile Leu Tyr Gln Gly Ala Ser Phe Arg Ser Leu Ser Ser
405 410 415

Asn Thr Glu Met Thr Leu Ser Ala Asn Thr Leu Gln Gln Leu Glu Val
420 425 430

Val Lys Asn Asn Ser Asp Gly Ser Glu Ser Gly Ser Leu Phe His Asn
435 440 445

Met Asn His Thr Leu Thr Val Tyr Gly Ser Arg Leu Leu Arg His Trp
450 455 460

Val Thr His Pro Leu Cys Asp Arg Asn Leu Ile Ser Ala Arg Leu Asp
465 470 475 480

Ala Val Ser Glu Ile Ser Ala Cys Met Gly Ser His Ser Ser Ser Gln
485 490 495

Leu Ser Ser Glu Leu Val Glu Glu Gly Ser Glu Arg Ala Ile Val Ser
500 505 510

Pro Glu Phe Tyr Leu Val Leu Ser Ser Val Leu Thr Ala Met Ser Arg
515 520 525

Ser Ser Asp Ile Gln Arg Gly Ile Thr Arg Ile Phe His Arg Thr Ala
530 535 540

Lys Ala Thr Glu Phe Ile Ala Val Met Glu Ala Ile Leu Leu Ala Gly
545 550 555 560

Lys Gln Ile Gln Arg Leu Gly Ile Lys Gln Asp Ser Glu Met Arg Ser
565 570 575

Met Gln Ser Ala Thr Val Arg Ser Thr Leu Leu Arg Lys Leu Ile Ser
580 585 590

Val Ile Ser Ser Pro Val Val Val Asp Asn Ala Gly Lys Leu Leu Ser
595 600 605

Ala Leu Asn Lys Glu Ala Ala Val Arg Gly Asp Leu Leu Asp Ile Leu
610 615 620

Ile Thr Ser Ser Asp Gln Phe Pro Glu Leu Ala Glu Ala Arg Gln Ala
625 630 635 640

Val Leu Val Ile Arg Glu Lys Leu Asp Ser Ser Ile Ala Ser Phe Arg
645 650 655

Lys Lys Leu Ala Ile Arg Asn Leu Glu Phe Leu Gln Val Ser Gly Ile
660 665 670

Thr His Leu Ile Glu Leu Pro Val Asp Ser Lys Val Pro His Asn Trp
675 680 685

Val Lys Val Asn Ser Thr Lys Lys Thr Ile Arg Tyr His Pro Pro Glu
690 695 700

Ile Val Ala Gly Leu Asp Glu Leu Ala Leu Ala Thr Glu His Leu Ala
705 710 715 720

Ile Val Asn Arg Ala Ser Trp Asp Ser Phe Leu Lys Ser Phe Ser Arg
725 730 735

Tyr Tyr Thr Asp Phe Lys Ala Ala Val Gln Ala Leu Ala Ala Leu Asp
740 745 750

Cys Leu His Ser Leu Ser Thr Leu Ser Arg Asn Lys Asn Tyr Val Arg
755 760 765

Pro Glu Phe Val Asp Asp Cys Glu Pro Val Glu Ile Asn Ile Gln Ser
770 775 780

Gly Arg His Pro Val Leu Glu Thr Ile Leu Gln Asp Asn Phe Val Pro
785 790 795 800

Asn Asp Thr Ile Leu His Ala Glu Gly Glu Tyr Cys Gln Ile Ile Thr
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Gly Pro Asn Met Gly Gly Lys Ser Cys Tyr Ile Arg Gln Val Ala Leu
820 825 830

Ile Ser Ile Met Ala Gln Val Gly Ser Phe Val Pro Ala Ser Phe Ala
835 840 845

Lys Leu His Val Leu Asp Gly Val Phe Thr Arg Met Gly Ala Ser Asp
850 855 860

Ser Ile Gln His Gly Arg Ser Thr Phe Leu Glu Glu Leu Ser Glu Ala
865 870 875 880

Ser His Ile Ile Arg Thr Cys Ser Ser Arg Ser Leu Val Ile Leu Asp
885 890 895

Glu Leu Gly Arg Gly Thr Ser Thr His Asp Gly Val Ala Ile Ala Tyr
900 905 910

Ala Thr Leu Gln His Leu Leu Ala Glu Lys Arg Cys Leu Val Leu Phe
915 920 925

Val Thr His Tyr Pro Glu Ile Ala Glu Ile Ser Asn Gly Phe Pro Gly
930 935 940

Ser Val Gly Thr Tyr His Val Ser Tyr Leu Thr Leu Gln Lys Asp Lys
945 950 955 960

Gly Ser Tyr Asp His Asp Asp Val Thr Tyr Leu Tyr Lys Leu Val Arg
965 970 975

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980 985 990

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995 1000 1005

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ccgtctggat ttaagccggc tgaatccgcc ggtgatgctt cgtccctgtt ctccaatatt 300

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gaacttagat cagtagaaga tataggagta gatggcgatg ttcctggtcc agaaacacca 540

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tctctctcac aattccaaaa a atg cag cgc cag aga tcg att ttg tct ttc      171
                        Met Gln Arg Gln Arg Ser Ile Leu Ser Phe
                         1               5                  10
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Ala Ala Ser Gly Gly Gly Gly Ser Gly Gly Pro Arg Phe Asn Val Arg
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gaa ggg gat gct aaa ggc gac gct tct gta cgt ttt gct gtt tcg aaa 315
Glu Gly Asp Ala Lys Gly Asp Ala Ser Val Arg Phe Ala Val Ser Lys
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tct gtc gat gag gtt aga gga acg gat act cca ccg gag aag gtt ccg 363
Ser Val Asp Glu Val Arg Gly Thr Asp Thr Pro Pro Glu Lys Val Pro
60 65 70

cgt cgt gtc ctg ccg tct gga ttt aag ccg gct gaa tcc gcc gst gat 411
Arg Arg Val Leu Pro Ser Gly Phe Lys Pro Ala Glu Ser Ala Gly Asp
75 80 85 90

gct tcg tcc ctg ttc tcc aat att atg cat aag ttt gta aaa gtc gat 459
Ala Ser Ser Leu Phe Ser Asn Ile Met His Lys Phe Val Lys Val Asp
95 100 105

gat cga gat tgt tct gga gag agg agc cga gaa gat gtt gtt ccg ctg 507
Asp Arg Asp Cys Ser Gly Glu Arg Ser Arg Glu Asp Val Val Pro Leu
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Asn Asp Ser Ser Leu Cys Met Lys Ala Asn Asp Val Ile Pro Gln Phe
125 130 135

cgt tcc aat aat ggt aaa act caa gaa aga aac cat gct ttt agt ttc 603
Arg Ser Asn Asn Gly Lys Thr Gln Glu Arg Asn His Ala Phe Ser Phe
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175 180 185

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Leu Lys Arg Val Leu Glu Asp Glu Met Thr Phe Lys Glu Asp Lys Val
190 195 200

cct gta ttg gac tct aac aaa agg ctg aaa atg ctc cag gat ccg gtt 795
Pro Val Leu Asp Ser Asn Lys Arg Leu Lys Met Leu Gln Asp Pro Val
205 210 215

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Cys Gly Glu Lys Lys Glu Val Asn Glu Gly Thr Lys Phe Glu Trp Leu
220 225 230

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Asp Ile Val Leu Phe Phe Lys Val Gly Lys Phe Tyr Glu Leu Tyr Glu
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315 320 325 330

gat gag gca gtg caa aag cta tta gct cgt gga tat aaa gtt gga cga 1179
Asp Glu Ala Val Gln Lys Leu Leu Ala Arg Gly Tyr Lys Val Gly Arg
335 340 345

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350 355 360

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380 385 390

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415 420 425

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495 500 505

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655 660 665

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700 705 710

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715 720 725 730

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735 740 745

ata ctt atc gaa ctt ttt atc gaa aga gca act caa tgg tct gag gtc 2427
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750 755 760

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765 770 775

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780 785 790

tca gaa gct aca gat cag aat cag aaa aca aaa ggg cca ata ctt aaa 2571
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795 800 805 810

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Ile Gln Gly Leu Trp His Pro Phe Ala Val Ala Ala Asp Gly Gln Leu
815 820 825

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Pro Val Pro Asn Asp Ile Leu Leu Gly Glu Ala Arg Arg Ser Ser Gly
830 835 840

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ctt ggc tgc tac gtg ccg tgt gag tct tgc gaa atc tcc ctc gtg gat      2811
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Ala Thr Gln Asp Ser Leu Val Ile Leu Asp Glu Leu Gly Arg Gly Thr
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Ser Thr Phe Asp Gly Tyr Ala Ile Ala Tyr Ser Val Phe Arg His Leu
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Leu Thr Lys Glu Phe Ala Ser His Pro Arg Val Thr Ser Lys His Met
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Gln Asp Leu Val Phe Leu Tyr Arg Leu Thr Glu Gly Ala Cys Pro Glu
        1005                1010                1015

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Ser Tyr Gly Leu Gln Val Ala Leu Met Ala Gly Ile Pro Asn Gln Val
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1070 1075 1080

aat gcc ccc att ggc gaa gat gac tac gac act ttg ttt tgc tta tgg 3435
Asn Ala Pro Ile Gly Glu Asp Asp Tyr Asp Thr Leu Phe Cys Leu Trp
1085 1090 1095

cat gag atc aaa tcc tct tac tgt gtt ccc aaa taaatggcta 3478
His Glu Ile Lys Ser Ser Tyr Cys Val Pro Lys
1100 1105

tgacataaca ctatctgaag ctcgttaagt cttttgcctc tctgatgttt attcctctta 3538

aaaaatgctt atatatcaaa aaattgtttc ctcgattaaa aaaaaaaaaa aaaaaaaaaa 3598

aaaaaaa 3606

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Ala Thr Thr Lys Gly Leu Val Ser Gly Asp Ala Ala Ser Gly Gly Gly
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Gly Ser Gly Gly Pro Arg Phe Asn Val Arg Glu Gly Asp Ala Lys Gly
35 40 45

Asp Ala Ser Val Arg Phe Ala Val Ser Lys Ser Val Asp Glu Val Arg
50 55 60

Gly Thr Asp Thr Pro Pro Glu Lys Val Pro Arg Arg Val Leu Pro Ser
65 70 75 80

Gly Phe Lys Pro Ala Glu Ser Ala Gly Asp Ala Ser Ser Leu Phe Ser
85 90 95

Asn Ile Met His Lys Phe Val Lys Val Asp Asp Arg Asp Cys Ser Gly
100 105 110

Glu Arg Ser Arg Glu Asp Val Val Pro Leu Asn Asp Ser Ser Leu Cys
115 120 125

Met Lys Ala Asn Asp Val Ile Pro Gln Phe Arg Ser Asn Asn Gly Lys
130 135 140

Thr Gln Glu Arg Asn His Ala Phe Ser Phe Ser Gly Arg Ala Glu Leu
145 150 155 160

Arg Ser Val Glu Asp Ile Gly Val Asp Gly Asp Val Pro Gly Pro Glu
165 170 175

Thr Pro Gly Met Arg Pro Arg Ala Ser Arg Leu Lys Arg Val Leu Glu
180 185 190

Asp Glu Met Thr Phe Lys Glu Asp Lys Val Pro Val Leu Asp Ser Asn
195 200 205

Lys Arg Leu Lys Met Leu Gln Asp Pro Val Cys Gly Glu Lys Lys Glu
210 215 220

Val Asn Glu Gly Thr Lys Phe Glu Trp Leu Glu Ser Ser Arg Ile Arg
225 230 235 240

Asp Ala Asn Arg Arg Arg Pro Asp Asp Pro Leu Tyr Asp Arg Lys Thr
245 250 255

Leu His Ile Pro Pro Asp Val Phe Lys Lys Met Ser Ala Ser Gln Lys
260 265 270

Gln Tyr Trp Ser Val Lys Ser Glu Tyr Met Asp Ile Val Leu Phe Phe
275 280 285

Lys Val Gly Lys Phe Tyr Glu Leu Tyr Glu Leu Asp Ala Glu Leu Gly
290 295 300

His Lys Glu Leu Asp Trp Lys Met Thr Met Ser Gly Val Gly Lys Cys
305 310 315 320

Arg Gln Val Gly Ile Ser Glu Ser Gly Ile Asp Glu Ala Val Gln Lys
325 330 335

Leu Leu Ala Arg Gly Tyr Lys Val Gly Arg Ile Glu Gln Leu Glu Thr
340 345 350

Ser Asp Gln Ala Lys Ala Arg Gly Ala Asn Thr Ile Ile Pro Arg Lys
355 360 365

Leu Val Gln Val Leu Thr Pro Ser Thr Ala Ser Glu Gly Asn Ile Gly
370 375 380

Pro Asp Ala Val His Leu Leu Ala Ile Lys Glu Ile Lys Met Glu Leu
385 390 395 400

Gln Lys Cys Ser Thr Val Tyr Gly Phe Ala Phe Val Asp Cys Ala Ala
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Leu Gly Ala Leu Leu Met Gln Val Ser Pro Lys Glu Val Leu Tyr Asp
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Ser Lys Gly Leu Ser Arg Glu Ala Gln Lys Ala Leu Arg Lys Tyr Thr
    450                 455                 460

Leu Thr Gly Ser Thr Ala Val Gln Leu Ala Pro Val Pro Gln Val Met
465                 470                 475                 480

Gly Asp Thr Asp Ala Ala Gly Val Arg Asn Ile Ile Glu Ser Asn Gly
                485                 490                 495

Tyr Phe Lys Gly Ser Ser Glu Ser Trp Asn Cys Ala Val Asp Gly Leu
            500                 505                 510

Asn Glu Cys Asp Val Ala Leu Ser Ala Leu Gly Glu Leu Ile Asn His
        515                 520                 525

Leu Ser Arg Leu Lys Leu Glu Asp Val Leu Lys His Gly Asp Ile Phe
    530                 535                 540

Pro Tyr Gln Val Tyr Arg Gly Cys Leu Arg Ile Asp Gly Gln Thr Met
545                 550                 555                 560

Val Asn Leu Glu Ile Phe Asn Asn Ser Cys Asp Gly Gly Pro Ser Gly
                565                 570                 575

Thr Leu Tyr Lys Tyr Leu Asp Asn Cys Val Ser Pro Thr Gly Lys Arg
            580                 585                 590

Leu Leu Arg Asn Trp Ile Cys His Pro Leu Lys Asp Val Glu Ser Ile
        595                 600                 605

Asn Lys Arg Leu Asp Val Val Glu Glu Phe Thr Ala Asn Ser Glu Ser
    610                 615                 620

Met Gln Ile Thr Gly Gln Tyr Leu His Lys Leu Pro Asp Leu Glu Arg
625                 630                 635                 640

Leu Leu Gly Arg Ile Lys Ser Ser Val Arg Ser Ser Ala Ser Val Leu
                645                 650                 655

Pro Ala Leu Leu Gly Lys Lys Val Leu Lys Gln Arg Val Lys Ala Phe
            660                 665                 670

Gly Gln Ile Val Lys Gly Phe Arg Ser Gly Ile Asp Leu Leu Leu Ala
        675                 680                 685

Leu Gln Lys Glu Ser Asn Met Met Ser Leu Leu Tyr Lys Leu Cys Lys
    690                 695                 700
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705 710 715 720

Phe Glu Ala Ala Ile Asp Ser Asp Phe Pro Asn Tyr Gln Asn Gln Asp
725 730 735

Val Thr Asp Glu Asn Ala Glu Thr Leu Thr Ile Leu Ile Glu Leu Phe
740 745 750

Ile Glu Arg Ala Thr Gln Trp Ser Glu Val Ile His Thr Ile Ser Cys
755 760 765

Leu Asp Val Leu Arg Ser Phe Ala Ile Ala Ala Ser Leu Ser Ala Gly
770 775 780

Ser Met Ala Arg Pro Val Ile Phe Pro Glu Ser Glu Ala Thr Asp Gln
785 790 795 800

Asn Gln Lys Thr Lys Gly Pro Ile Leu Lys Ile Gln Gly Leu Trp His
805 810 815

Pro Phe Ala Val Ala Ala Asp Gly Gln Leu Pro Val Pro Asn Asp Ile
820 825 830

Leu Leu Gly Glu Ala Arg Arg Ser Ser Gly Ser Ile His Pro Arg Ser
835 840 845

Leu Leu Leu Thr Gly Pro Asn Met Gly Gly Lys Ser Thr Leu Leu Arg
850 855 860

Ala Thr Cys Leu Ala Val Ile Phe Ala Gln Leu Gly Cys Tyr Val Pro
865 870 875 880

Cys Glu Ser Cys Glu Ile Ser Leu Val Asp Thr Ile Phe Thr Arg Leu
885 890 895

Gly Ala Ser Asp Arg Ile Met Thr Gly Glu Ser Thr Phe Leu Val Glu
900 905 910

Cys Thr Glu Thr Ala Ser Val Leu Gln Asn Ala Thr Gln Asp Ser Leu
915 920 925

Val Ile Leu Asp Glu Leu Gly Arg Gly Thr Ser Thr Phe Asp Gly Tyr
930 935 940

Ala Ile Ala Tyr Ser Val Phe Arg His Leu Val Glu Lys Val Gln Cys
945 950 955 960

Arg Met Leu Phe Ala Thr His Tyr His Pro Leu Thr Lys Glu Phe Ala
965 970 975

Ser His Pro Arg Val Thr Ser Lys His Met Ala Cys Ala Phe Lys Ser
980 985 990

Arg Ser Asp Tyr Gln Pro Arg Gly Cys Asp Gln Asp Leu Val Phe Leu
995 1000 1005

Tyr Arg Leu Thr Glu Gly Ala Cys Pro Glu Ser Tyr Gly Leu Gln Val
1010 1015 1020

Ala Leu Met Ala Gly Ile Pro Asn Gln Val Val Glu Thr Ala Ser Gly
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Ala Ala Gln Ala Met Lys Arg Ser Ile Gly Glu Asn Phe Lys Ser Ser
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Glu Leu Arg Ser Glu Phe Ser Ser Leu His Glu Asp Trp Leu Lys Ser
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Leu Val Gly Ile Ser Arg Val Ala His Asn Asn Ala Pro Ile Gly Glu
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Tyr Cys Val Pro Lys
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accatgcata gcttaaactt cttg 24

<210> 33
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<220>
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<400> 33

acataaccac aaataggggt gc 22

<210> 34
<211> 18
<212> DNA
<213> Artificial sequence

<220>
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<400> 34

gaagcgatat tgttcgtg 18

<210> 35
<211> 18
<212> DNA
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<220>
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<400> 35

agattgcgag aacattcc 18

<210> 36
<211> 31
<212> DNA
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<220>
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<400> 36

acgcgtcgac tcagctatga gattactcgt g 31

<210> 37
<211> 29
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<220>
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gctctagatt tctcgctcta agactctct 29

<210> 38
<211> 32
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<220>
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<400> 38

gctctagagc ttctcttaag taagtgattg at 32

<210> 39
<211> 48
<212> DNA
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<220>
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<212> DNA
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<220>
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<400> 40

acgcgtcgac gaattcgcaa gtgggg 26

<210> 41
<211> 38
<212> DNA
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<220>
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tccatggaga tctcccgggt accgatttgc ttcgaggg 38

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<220>
<223> Forward primer for PCR amplification of ATEAT1 SSLP marker in Arabidopsis thaliana subspecies

<400> 42

gccactgcgt gaatgatatg 20

<210> 43
<211> 22
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<220>
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<400> 43

cgaacagcca acattaattc cc 22

<210> 44
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aaccaaggca cagaagcg 18

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<211> 18
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acccaagtga tcgccacc 18

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tctgtatctc ggtgaattct cc 22

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ggtctgttga tgtcgtaagt cg 22

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ctgatctcac ggacaatagt gc 22

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ggctccataa aaagtgcacc 20

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ctccagttgg aagctaaagg g 21

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tgttttttag gacaaatggc g 21

<210> 54
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ccttcacatc caaaacccac 20

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gcacataccc acaaccagaa 20

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cgctacgctt ttcggtaaag 20

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gcacagtcca agtcacaacc 20

<210> 58
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aaagagatga gaatttggac 20

<210> 59
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acatatcaat atattaaagt agc 23

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tcgtctactg cactgccg 18

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gaggacatgt ataggagcct cg 22

<210> 62
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<400> 62

tgacctcctc ttccatggag 20

<210> 63
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ttaacagaaa cccaaagctt tc 22

<210> 64
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aggcaaatgt ccatttcatt g 21

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acgacatggc agatttctcc 20

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agctgcttcc ttatagcgtc c 21

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catccgaatg ccattgttc 19

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gaaaaaacgc tactttcgtg g 21

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caagagcaat atcaagagca gc 22

<210> 70
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catgcaattt gcatctgagg 20

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ctctgtcact cttttcctct gg 22

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<400> 72

tggatttctt cctctcttca c 21

<210> 73
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atggagaagc ttacactgat c 21

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aatgttgtcc tcccctcctc 20

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tgatgctctc tgaaacaaga gc 22

<210> 76
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gagggcaaat ctttatttcg g 21

<210> 77
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tggctttcgt ttataaacat cc 22

<210> 78
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gcgaaaaaac aaaaaaatcc a 21

<210> 79
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cgacgaatcg acagaattag g 21

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gaaatccaaa tcccagagag g 21

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tctccccact agttttgtgt cc 22

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<400> 82

taccgtcaat ttcatcgcc 19

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ggatccctaa ctgtaaaatc cc 22

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aatcccagta accaaacaca ca 22

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cccagtctaa ccacgaccac 20

<210> 86
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gttttgggaa gttttgctgg 20

<210> 87
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<400> 87

cagtctaaaa gcgagagtat gatg 24

<210> 88
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gttatggagt ttctagggca cg 22

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tgccccattt tgttcttctc 20

<210> 90
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agagctacca gatccgatgg 20

<210> 91
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<400> 91

ggtttcgttt cactatccag g 21

<210> 92
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<400> 92

ggagaaaatg tcactctcca cc 22

<210> 93
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<212> DNA
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<400> 93

aggcatggga gacatttacg 20

<210> 94
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<220>
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<400> 94

ctccaccaat catgcaaatg 20

<210> 95
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tgatgttgat ggagatggtc a 21

<210> 96
<211> 22
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<223> Forward primer for PCR amplification of NGA129 SSLP marker in Arabidopsis thaliana subspecies

<400> 96

tcaggaggaa ctaaagtgag gg 22

<210> 97
<211> 22
<212> DNA
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<220>
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<400> 97

cacactgaag atggtcttga gg 22

<210> 98
<211> 8062
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<220>
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<400> 97

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